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ANNOUNCEMENT

The next number of the **Medical Clinics of North America** will be published in September and will be the *Philadelphia Number*. It will contain clinics by the following:

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THE MEDICAL CLINICS
OF
NORTH AMERICA

VOLUME 1 NUMBER 1

CLINIC OF DR. THEODORE C. JANEWAY

JOHNS HOPKINS HOSPITAL

HODGKIN'S DISEASE WITH EXTENSIVE SKIN ERUPTION

Demonstration of Patient. Discussion of the Skin Lesions Associated with the Leukemia and Hodgkin's Disease. Treatment by Radiation with Radium. Demonstration of Remarkable Improvement Five Weeks Later. The More Important Literature of Hodgkin's Disease and of the Leukemic and Allied Skin Lesions.

February 3, 1917.

DR. JANEWAY: We have today an interesting case illustrating a very rare but characteristic association of two morbid conditions. Mr. Sanger will give the history of the case.

MR. SANGER: Patient, L. C. (Med. No. 37,368), aged thirty-six. Occupation, farmer. Admitted to Ward E January 26, 1917.

Personal History.—Always a hard-working man. Measles and whooping-cough in childhood. Malaria at nineteen, cured after three weeks' treatment and never recurring since. He has had recurrent persistent headaches which have continued since the present illness began. The only other finding in the personal history is nycturia for ten years, about three times a night.

Present Illness.—Began ten months ago with symmetric lesions on the forearm about 6 cm. above the wrist. These lesions were more or less papular and caused a good deal of

itching. They spread rapidly all over the body. About three weeks later he noticed above the left clavicle swellings which he associated with glandular enlargement. These continued to grow, at first only on the left side. The patient noticed increasing weakness. The glands on the right side were not enlarged until recently. In the meantime the skin changes have spread all over the body, the head, scalp, chest, back, arms, and legs being covered with scratch-marks and blood crusts, indicating tremendous itching, with marked excoriation of the skin.

Dr. Janeway: To sum up the story—Mr. C., previously a healthy farmer down in South Carolina, came to Baltimore last week to consult Dr. Gilchrist because of a severe skin eruption and itching, giving the history that ten weeks ago he noticed the first lesions as little papules on the skin of the forearms; that from the first they were associated with intense itching; that there followed a fairly rapid development of similar lesions over the skin of practically the entire body, with some even on the face. Were any parts of the body exempt?

Mr. Sanger: The palms of the hands, the soles of the feet, and the genitalia.

Dr. Janeway: These parts, then, were exempt, but every other portion of the body, including the scalp, was the seat of most intense itching and of small, not very deep-colored papules. Three weeks after the first itching lesions appeared on the forearms he noticed swellings above the left clavicle, and states that during the ten months of progressive development of the itching eruption there has been progressive enlargement of the glands of the left side of the neck, and much more recently enlargement of those on the right side of the neck. He has not noticed enlargements anywhere else.

Mr. Sanger: I should have mentioned that the patient has had a harassing cough for about two months.

Dr. Janeway: For two months he has had a paroxysmal cough, which from his description we would call a brassy cough, and a little tendency to shortness of breath on exertion. Also during the last few months his strength has been failing somewhat. Has there been any pallor or loss of weight?

MR. SANGER: He has not noticed pallor. His weight in the past has been 160 pounds; for the last three years he has weighed 140 pounds.

DR. JANEWAY: The patient, then, comes in weighing his average for the last three years. I saw the patient first in the dermatologic clinic with Dr. Gilchrist. He was sent from there to the ward for observation and treatment, and the condition then was as it is shown now except that there has been some amelioration in the itching with a little less scratching. The lesions on admission were of exactly the kind visible now, but much greater in extent. What are those lesions?

MR. SANGER: The skin lesions are to be classed as of three types. There is a papular eruption over the face, hands, scalp, chest, back, and legs which has a tendency to grouping. These papules are covered with blood crusts, with excoriation of the skin. Then there is diffuse pigmentation all over the body. There is also a third type of lesion, a definite thickening of the skin on the dorsum of the hands, which the patient has noticed since the onset of the present illness.

DR. JANEWAY: In addition, there are the universal scratch-marks everywhere the patient could reach, and he has been pretty successful in reaching every portion of his body. The shoulders are usually most exempt, over the scapula, just below the spine, where one cannot reach from above or very well from below. But there is very little free area anywhere on the patient's body. The skin over the latissimus dorsi seems to be freer from eruption than that of any part of the body. You will notice here on the trunk the characteristics of the eruption. In the first place, as Mr. Sanger has said, there are these papules, 2 or 3 mm. across, none of them very large, with a slight tendency toward grouping—in large areas coalescent, where they are the seat of the most intense itching. There is, in addition, an extensive pigmentation, which is quite obviously the remains of lesions that have run their course. One sees evidences of scratching at the center of many of these pigmented macules, and over the abdomen the pigmentation is particularly diffuse. But the brown areas, I think, are to be interpreted as the site

of previous papular lesions with excoriation, and where the excoriation has gone deep it has been associated with some infection.

MR. SANGER: Some writers think that the pigmentation is probably due to involvement of the retroperitoneal glands.

DR. JANEWAY: But the pigmentation occurs where the infection has been. It seems to me unnecessary to assume that it is independent. One sees exactly the same pigmentation in practically all skin eruptions that lead to scratching over this period of time. So far as the pigmentation goes, the papules and the scratch-marks about the papular lesions might lead one to the erroneous diagnosis of what condition?

MR. SANGER: Prurigo.

DR. JANEWAY: That would be one possibility in diagnosis that would account not only for the pigmentation of the scratch-marks but also for the papular lesions. It is a more or less typical prurigo, though not the true prurigo of Hebra, but that is largely because of the difference in association. What other condition might give you a picture similar to the one we have here—of course, a much commoner one?

MR. SANGER: Scabies.

DR. JANEWAY: What about pediculosis or the vagabond type of pigmentation? One sees vagabonds' disease looking so much like this at a distance that it would be easy to be deceived. We see little of the disease here, but I was very familiar with it in the City Hospital, New York, where we had the lowest class of the population coming in. There was one very famous patient in Bellevue. When he was washed by the nurse one layer after another of what was apparently skin came away. It appeared that for eight years he had not washed and had not changed his clothes, but when his underclothes began to wear out he put on another suit over them, and it was exceedingly difficult for a number of weeks to tell just when one had reached the epidermis. In vagabonds' disease, when you get down through the successive layers of covering you get exactly similar scratch-marks and pigmentation to those seen here, but, as a rule, the pigmentation is very diffuse over the portions of the

body where the clothes were tightest, particularly around the waist and about the shoulders, and the face always escapes. Also the arms would tend to show rather fewer lesions than they do in this case.

Now the third element is the thickening of the skin of the hands, which the patient is sure has come on quite recently. He works out-of-doors and in the sun. He has the palms that go with outdoor labor—very thick skin, but not the rough, fissured, and perfectly dry skin which he has on the dorsum of the hand. Do you interpret this, Mr. Sanger, as really a part of the lesion?

MR. SANGER: In some of the cases thickening of the skin of the hands has been noticed.

DR. JANEWAY: Is it an essential part of the lesion? Is there anything corresponding to it on the dorsum of the foot?

MR. SANGER: No.

DR. JANEWAY: The dorsum of the foot shows absolutely nothing corresponding to the condition of the hand. I question how much of that is of long standing and due to his occupation and how much to the present condition. There are certainly none of the typical lesions there, but it is an interesting possible association. In addition to the skin eruption, what are the other features?

MR. SANGER: The collar of glands above both clavicles is very prominent, but more especially on the left.

DR. JANEWAY: This collar of glands is very evident on the left and only slightly evident on the right side of the neck, and the individual lymph-nodes stand out clearly even from a distance. This is not a single tumor mass or a mass of confluent lymph-nodes. The lymph-nodes are perfectly discrete, varying in size from that of a bean to that of a hazelnut or walnut. What is their consistency?

MR. SANGER: They are quite hard, but were much harder on admission than they are now

DR. JANEWAY: They were distinctly harder on admission. They have about the consistency of good thick rubber. They are not absolutely firm, but have just about the elasticity of

a similar amount of rubber. The glands are absolutely non-adherent either to the skin or to the underlying structures.

MR. SANGER: Or to each other.

DR. JANEWAY: In addition to these large visible lymph-nodes there are smaller nodes in the axillæ. Especially in the right axilla this chain can be traced to below the clavicle, and there is one large mass below the left clavicle. The epitrochlears are about the size of large beans; the inguinals are enlarged, but not more than we see in many people with no general cause for the enlargement. Is there any evidence of enlargement of the internal lymph-nodes?

MR. SANGER: I think there is definite retrosternal dulness over an area about 3 cm. in diameter, a little more to the left, and in the back over the first two dorsal spines.

DR. JANEWAY: Do you ordinarily expect a good resonant percussion-note over the three upper thoracic spines?

MR. SANGER: Not as good as one gets over the lower.

DR. JANEWAY: I don't think you can reason from dulness over the upper thoracic spines; that is, not above the third. Down to the third you expect to have a rather feeble resonance transmitted. I am perfectly frank in confessing that I have not been able to convince myself of the existence, from the patient's back, of any evidence of a solid mass in the mediastinum. That doesn't mean that such a mass is not there, but I haven't the proof of it on physical examination. I am entirely willing to let the *x*-ray make the diagnosis, but not to let it make the physical examination for me. As to the retrosternal dulness, the evidence is a little more conclusive. Certainly one gets a very definite, wide area of retromanubrial dulness. This has been measured in the ward, and is about 6 cm. to the right and 4 or 5 cm. to the left.

MR. SANGER: Absolute dulness about 5 cm. each side and relative dulness about 4 cm. each side of that area.

DR. JANEWAY: There is certainly well-marked dulness—and one can percuss out only well-marked dulness in this audience—5 cm. to the right and 4.5 cm. to the left. The radiograph, as you can see, demonstrates a large, sharply outlined mass

above the heart shadow, which Dr. Baetjer considers typical of thoracic Hodgkin's disease, and a clouding of the root of the neck due to the much enlarged cervical lymph-nodes. In addition, has he any enlargement of the spleen or liver?

MR. SANGER: Neither are palpable. The splenic dulness goes to the costal margin.

DR. JANEWAY: I have been unable to detect any enlargement of the spleen. The liver edge comes rather well below the costal

Fig. 1.—Radiograph No. 44,025 taken January 29th, 1917, before radiotherapy.

arch on full inspiration, but certainly there is no considerable enlargement. With such a skin eruption, associated with enlargement of the lymph-nodes, the two developing practically parallel with one another—the skin eruption being the first thing to call the attention of the patient to his illness—what diagnoses would occur to you before you had the opportunity of examining further?

MR. SANGER: Leukemia is often associated with such a

skin eruption and glandular enlargement, but the blood-picture would be needed for this diagnosis.

Dr. Janeway: But preliminary to the blood-picture you would reduce the possibilities to a very few diseases, particularly to two. What would those be; that is, if you were familiar with the descriptions in the literature of the association of this particular type of skin lesion with general diseases? What two diseases would come to your mind at once, the differentiation between which would have to rest upon the blood examination?

Mr. Sanger: Leukemia and pseudoleukemia.

Dr. Janeway: By what name do we know the latter?

Mr. Sanger: Hodgkin's disease.

Dr. Janeway: What type of leukemia is associated with skin lesions?

Mr. Sanger: Lymphatic leukemia.

Dr. Janeway: On the basis of the physical examination, I think one could almost rule out lymphatic leukemia without an examination of the blood. What is an essential part of the picture of a chronic lymphatic leukemia?—for the condition here can only be chronic, with a skin of this type and a ten months' history.

Mr. Sanger: Enlargement of the liver and spleen.

Dr. Janeway: Does this in lymphatic leukemia reach the degree that one finds in myeloid leukemia?

Mr. Sanger: I do not think it does.

Dr. Janeway: No. As a rule in lymphatic leukemia the spleen comes about to the level of the umbilicus, very rarely below, whereas in myeloid leukemia after ten months the spleen might be down to the iliac crest. There is a great difference in the degree of splenic enlargement in the two types of leukemia. That a patient with chronic lymphatic leukemia could have a large collar of glands and a ten months' history, without a spleen which can be felt, I think almost out of the question. In acute leukemia, of course, one may miss all the external manifestations of the disease, but the clinical picture in that case is totally different from the one we have here. The blood examination, however, gives us the final clue:

On Admission.			*After Radiation.*	
R. B. C.	5,820,000			
W. B. C.	25,400		W. B. C.	25,400
P. M. N.	89.0 per cent.	Platelets increased	P. M. N.	92.0 per cent.
P. M. E.	0.6 "	in number and	P. M. E.	0.4 "
S. M.	1.4 "	size.	S. M.	1.0 "
L. M.	3.0 "		L. M.	3.3 "
Tr.	6.0 "		Tr.	3.3 "

We have been over the question of the significance of the blood-picture so recently that it is unnecessary to say much more about it here. This picture conforms exactly to the picture which Bunting describes as that of late Hodgkin's disease—marked polymorphonuclear leukocytosis, very marked diminution in the definite lymphatic elements of the blood, a marked increase in polynuclears, and a gain in mononuclears which are not of lymphatic origin, particularly the so-called transitional cells. Here, therefore, is not merely negative evidence ruling out a lymphatic leukemia, but very strong positive evidence arguing for the existence of Hodgkin's disease. Is it then possible that some of the polynuclear leukocytosis is due to infection of many of these skin lesions, or are similar polynuclear percentages seen in Hodgkin's disease without any other cause for the leukocytosis?

MR. SANGER: This is not at all uncommon in the late cases.

DR. JANEWAY: We have made the diagnosis reasonably certain then. What further has been done?

MR. SANGER: Last Tuesday Dr. Dunn extirpated a gland just above the episternal notch. A section was made and was found by Dr. Bloodgood to contain an increase of eosin-staining fibrous tissue, a decrease in the lymphoid elements, quite a number of eosinophils, and many endothelial cells of undoubted giant type.

DR. JANEWAY: The endothelioid giant cell, known in the literature as the Dorothy Reed cell, is very typical of Hodgkin's disease. This is a characteristic picture—an extensive loss of lymphoid cells, a marked increase in the fibrous tissue, the presence of numbers of these so-called endothelioid giant cells. These are not multinuclear giant cells, but very large cells of

endothelial type, with a large single nucleus. Also characteristic is the presence of many eosinophils in the gland, which is not a constant feature, but a very important finding when present. The presence of mast-cells in the gland is also of interest. There was no sign of invasion through the capsule. In addition, Dr. Guthrie has made a smear of the gland, and perhaps he will say a word about his findings.

DR. GUTHRIE: The smear showed the expected findings one would consider positive in the section, only it was possible by the use of an oil immersion to define a large number of the cells. There were the Dorothy Reed cells, an increase in the eosinophils, a small number of lymphoid elements, and an increase in the mast-cells.

DR. JANEWAY: It is interesting, and will be of value in the future in the more rapid diagnosis of these cases, that Dr. Guthrie was able in a smear from the gland removed to obtain perfectly valid evidence of the existence of the tissue elements which are increased in Hodgkin's disease, and the disappearance of the lymphoid elements which should be present in normal or hyperplastic lymph-nodes, so that a diagnosis was made as quickly as by a blood examination. The cells are easily seen in the smear, and the method will be well worth trying out in the future. Altogether the diagnosis seems perfectly clear, and treatment has already been instituted. What drug is the only one that has ever been of much benefit in these cases?

MR. SANGER: Compounds of arsenic.

DR. JANEWAY: I have seen cases in which arsenic gave very brilliant temporary results with rapid subsidence of the visible lymph-node swellings. On the other hand, we have a method now which is so much more rapid and certain in its results that we resort to it at once in these cases, and that is—

MR. SANGER: Radiotherapy.

DR. JANEWAY: Accumulated experience with the use of radium and of the *x*-ray seems rather favorable to radium and against *x*-ray treatment. The dangers apparently are much less from burns, and the effect from a single radiation seems to be much greater than can be obtained with any safety with the

x-ray. The patient was radiated by Dr. Burnam on Thursday, two days ago.

MR. SANGER: On account of being very nervous the patient was given only an eight-hour radiation instead of one of fifteen hours.

DR. JANEWAY: He received an eight-hour radiation over the neck and chest. The chest was radiated, not merely on account of suspicious evidence in the physical examination and the brassy cough, but also because of the very clear evidence in the *x*-ray picture (*x*-ray shown) of this sharply outlined mass in the mediastium, lying definitely above the heart, separable from the aortic shadow and quite different from it because of the clean-cut margins, which do not occur with any pulsating organ—a mass which extends farther to the right than to the left, but which merges above the clavicle and sternum into the shadow in the lower left neck, due to the mass of lymph-nodes there. The evidence here is very much greater than I should have assumed from my physical examination, which, however, showed definite restrosternal dulness. Has he had any difficulty in swallowing?

MR. SANGER: None at all.

DR. JANEWAY: The blood-count since radiation shows no important change, but one would not expect any striking effects in this length of time. Perhaps in a week's time we may expect greater effects. Dr. Bloomfield tells me that the patient shown before the class last year with very marked Hodgkin's disease, mainly cervical and mediastinal, and who was treated with radium, has remained absolutely well. There was also a patient, a girl, treated nearly two years ago, who had the most extreme thoracic Hodgkin's disease, with very marked involvement of the pleura on one side, and who was well at the end of a year, but is now dead after a relapse. She had been treated with *x*-rays several years previously, and had a long subsidence of symptoms before her admission here in the spring of 1915, and a remission of about a year after the radium treatment at that time.

I shall say a few words about the occurrence of skin eruptions in connection with diseases of the hemopoietic and lymphatic

systems. While these diseases are rare, they are of very great interest, because thay belong in the borderland between external and internal medicine, between dermatology and clinical medicine, where it is most important to be awake to both points of view. The earliest description of a skin eruption in leukemia and in Hodgkin's disease dates back before the 70's of the last century, and the observations did not begin to accumulate in any great number until about twenty years ago. The whole question has perhaps been summed up better by Pinkus than by anyone else, both from individually observed cases of his own and from cases in the literature. He reached the conclusion that the skin eruptions of leukemia, and what was then called pseudoleukemia, but which we know as Hodgkin's disease, fell into three groups: First, the definite leukemic tumors of the skin, which are similar in their histologic structure to the leukemic infiltrations of the internal organs, and which are not new growths in the strict sense, but leukemic infiltrations occurring in the skin and going on to tumor formation. Then a second type, first studied and described by Kaposi as what he called "lymphodermia perniciosa," and which has come down in the literature as Kaposi's disease. Kaposi says this type is characterized first by the development of an exudative eruption, that is, a more or less diffuse dermatitis, with much redness, burning, and itching of the skin, and then later by a papular stage, and eventually by the development of tumors of the skin, which are quite similar to the lymphoid skin tumors occurring without the primary stage of dermatitis. The third type is the one we have here today, a type which occurs more frequently with Hodgkin's disease, I think, than with leukemia. The eruption is not of any single kind. Characteristic of this type is the occurrence, usually very early, and frequently before the appearance of any other evidences, of an exudative eruption, that is, an eruption which is manifested either as an erythrodermia, as an urticaria, or, as in this case and perhaps most commonly, as prurigo papules with intense itching. In Hodgkin's disease this prurigo is perhaps the most frequent of the eruptions. Attention was called to it by Rolleston in 1909. A review by Alexander, which is more recent

than Rolleston's work, is based on the study of an accumulated mass of material and tends to bring these three groups together. The end stages of Kaposi's disease are in no way distinguishable from the ordinary leukemic tumors of the skin. The early stages are quite similar to the cases of erythrodermia, or eczema, eruptions which sometimes do not go on to the formation of tumors, so that this type is intermediate between the true skin tumors and these associated exudative eruptions. At least one may make the distinction between two straightforward types: (1) True leukemic involvement of the skin, or in very rare cases granulomatous tumors of the skin in Hodgkin's disease; (2) exudative eruptions, urticaria, erythrodermia, or prurigo, which cannot be brought into definite relation with the underlying disease, but which seem to have a clear-cut clinical association with it, and, therefore, must be indirectly related to it. These forms have not the histologic structure of the other lesions of the disease, but are very definitely associated with them, though they frequently occur with other diseases. The important thing to remember is that a few cases of Hodgkin's disease, probably not more than 3 or 4 in every 100, and possibly even fewer, begin with one of these eruptions. Therefore the disease may be wholly overlooked by the dermatologist—the real disease from which the patient suffers—if his interest is centered solely on the description and classification in a proper pigeon-hole of the skin lesion which presents itself to him. Second, the medical man may be equally careless in failing to report and call attention to the occurrence of skin lesions in cases of Hodgkin's disease or leukemia, because he has so little knowledge of dermatology that he centers his whole interest on what to him is important, the source of the disease, and passes by the skin eruption as not of much consequence.

We must take a middle ground between these two viewpoints, and clinicians must become interested in this particular borderland, because it is from these cases that we shall get a larger insight into the etiology of the dermatoses and shall be able to contribute something toward putting dermatology on a more scientific basis along with some of the other branches of clinical

medicine—not many by any manner of means, because much of clinical medicine, like dermatology, is still in the stage of description and classification. But we are now approaching disease from the standpoint of etiology. In spite of Bunting's and Yates' work, this cannot be considered solved for Hodgkin's disease. Some dermatologists are studying from that standpoint this perfectly clean-cut group of skin manifestations in association with diseases of the blood-forming and lymphatic systems. I should advise you to study some of the works of which the references are on the blackboard.[1] There is one article, by Mariani, which is perhaps the most extensive investigation in this field, Mariani goes from scrofula and tuberculosis, on the one hand, to acute leukemia on the other, and has worked all into a scheme of blocks and circles and cross-lines, so that when he gets through there isn't any difference between the skin tuberculids and the prurigo eruption of Hodgkin's disease. They can all be brought together in his mind. Of course one of the main causes for this view is the persistence on the Continent of Europe of the teaching, for which Sternberg is chiefly responsible, that after all Hodgkin's disease is nothing but a peculiar and modified form of tuberculosis. This we do not subscribe to, but consider Hodgkin's disease an infectious granuloma of the lymphatic system of wholly unknown etiology, but of a very precise histology, which we do know, largely through the work of Dorothy Reed and of Longcope.

And now a word in regard to the other side of the problem. The leukemic skin tumors resemble more or less the true multiple sarcomata of the skin, which, however, are clinically and histologically distinguishable. Again, the granulomatous skin lesions of Hodgkin's disease have many points of likeness to such diseases as mycosis fungoides, possibly to conditions of such clear-cut etiology as yaws. All these similarities suggest many points of interest in the study of the still perfectly obscure etiology of Hodgkin's disease.

I hope to show the patient at some subsequent clinic when we may observe the further effect of his radiotherapy.

[1] See Bibliography (pp. 15, 16).

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March 3, 1917.

Dr. Janeway: Mr. Sanger's patient was shown you five weeks ago, with a remarkable prurigo-like skin eruption with pigmentation and tremendously enlarged lymph-nodes. The diagnosis of Hodgkin's disease was made, both on the basis of the clinical features and the blood-picture. What treatment, Mr. Sanger, has been given?

Mr. Sanger: Radiation has been the only treatment—the first radiation on the 26th of February. Immediately following there was a transient rise in the blood-count to 27,000.

Dr. Janeway: With a fall of lymphocytes to 0.6 per cent.—a most extraordinary disappearance of lymphoid elements in

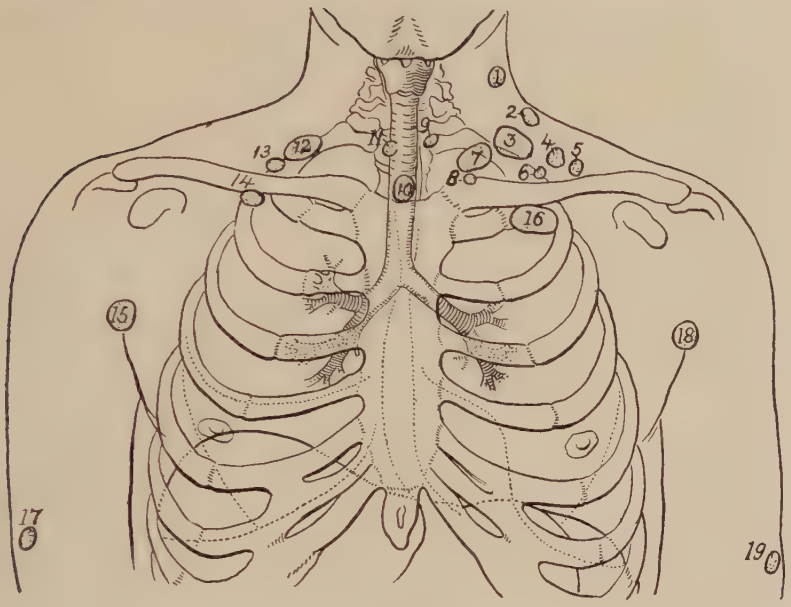

Fig. 2.

GLAND MEASUREMENTS BEFORE AND AFTER RADIATION

Gland No.	January 28.	February 12.	March 3.
1.....	2.5 x 2 cm.	1.4 x 1.2 cm.	1 x 1 cm.
2.....	2.4 x 1.7 cm.	1.8 x 1.4 cm.	1.6 x 1.5 cm.
3.....	5.0 x 3.5 cm.	3.5 x 2.7 cm.	2.9 x 2.4 cm.
4.....	1.5 x 1.5 cm.	1.8 x 1.8 cm.	Small.[1]
5.....	1 x 1 cm.	1.2 x 1.2 cm.	Small.
6.....	Small.	Small.	Small.
7.....	3.8 x 4 cm.	2.3 x 2 cm.	2 x 1.5 cm.
8.....	Small.	Small.	Small.
9.....	1.5 x 1 cm.	Small.	Small.
10.....	2.3 x 2 cm.	Small.	Small.
11.....	1.1 x 1 cm.	Excised.	Excised.
12.....	3.6 x 2.8 cm.	2.4 x 2 cm.	2.4 x 2 cm.
13.....	Small.	Small.	Small.
14.....	2.1 x 1.6 cm.	Gone.	Gone.
15.....	Larger than No. 18.	Small.	Not palpable.
16.....	3.5 x 2.8 cm.	3 x 2 cm.	Gone.
17.....	Bean-sized.	Same.	Same.
18.....	Smaller than No. 15.	Small.	Small.
19.....	Bean-sized.	Same.	Same.

[1] Palpable, but too small to measure. January 31st, ten hours' radiation; February 25th, eight hours' radiation.

the blood. With the fall in the blood-count what clinical improvement took place in the glands?

Mr. Sanger: A week after the radiation the glands were appreciably softer and smaller. By February 26th they were measurably smaller.

Dr. Janeway: There has been a striking subsidence in the size of the glands, visible to the naked eye, from week to week.

Fig. 3.—Radiograph No. 44,669 taken February 23, 1917, twenty-three days after radiotherapy.

The enlarged glands on the right side of the neck have almost entirely disappeared, while those on the left side are much smaller and very freely movable. Only a small group at the root of the neck on the left side and one gland near the sternoclavicular joint are now appreciable. All the others have receded to practically normal size, have they not?

MR. SANGER: The axillary glands are not palpable this morning. The epitrochlears are still about the same size, but they have not received radiation.

DR. JANEWAY: The reduction in the size of the mediastinal mass can be readily seen on comparing this radiograph, taken February 23d, with the original picture of January 29th. In addition, the clouding of the root of the neck, so noticeable in the former picture, has now quite disappeared with the reduction in size of the cervical lymph-nodes. Has there been further improvement since the 26th of February?

MR. SANGER: There has been nothing noticeable since that time. The blood-picture is essentially a normal picture except for a continuing high transitional count.

TABLE 1

THE JOHNS HOPKINS HOSPITAL

J. H. H.—Medical No. 37,368.

Date.	Hgb.	R. B. C.	W.B.C.	Polymorphonuclears.			Mononuclears.		Transitionals.	Platelets.
				Neutr.	Eosin.	Bas.	Small.	Large.		
	%			%	%	%	%	%	%	
Jan. 26...	76	5,820,000	25,400	89.0	0.6	0	1.4	3.0	6.0	++
31 Radiation.	87	5,940,000	23,800	88.6	0.4	0	3.0	2.4	5.6	++
Feb. 1...	.....	.....	22,800	93.2	0.2	0	1.8	2.0	2.8	+
5...	89	6,220,000	27,000	90.0	0.5	0	1.0	4.0	4.5	++
6...	.....	.....	19,200	82.0	1.0	0	3.0	8.0	6.0	−
7...	.....	.....	20,000	83.0	0	0.5	3.0	6.0	7.5	++
8...	.....	.....	10,400	85.5	0.5	0	4.5	2.5	7.0	+
9...	82	6,362,000	10,440	81.5	0	0.5	6.0	5.0	7.0	+
15...	85	.....	8,350	77.0	1.0	0.5	6.0	5.0	12.0	+
23...	85	5,896,000	9,960	79.4	1.0	0	6.4	2.6	10.6	+
26 Radiation.	85	5,648,000	10,000	84.5	0.5	0	2.0	4.0	9.0	About normal.
Feb. 28...	.....	.....	9,400	83.0	0	0	5.5	3.0	8.5	About normal.
Mar. 2...	.....	.....	10,200	85.0	0	0	7.0	3.5	4.5	−
7...	.....	.....	7,300	85.0	0.5	0	4.0	3.0	7.5	−
9...	.....	.....	5,000	80.0	1.0	0	4.0	4.0	11.0	−
12...	89	5,344,000	6,000	77.0	0	0	7.0	4.0	12.0	−

DR. JANEWAY: Aside from this the count is normal. The patient had no anemia in spite of his ten months' disease. Do you interpert the disappearance of the skin eruption as associated solely with the decrease in the size of the glands under radiation?

MR. SANGER: The skin lesions had begun to disappear before radiation.

DR. JANEWAY: It is clear that putting the patient to bed, where there is no friction of clothing against his body, and using calamine lotion on his hands and menthol on his body, have resulted in a disappearance of the prurigo-like eruption. We have eliminated the constant irritation from his own scratching, and though we cannot say that this disappearance has been due only to the local treatment, this has played a part. I think it probable, however, that if he had not received radiation he would have had a recurrence of the lesion. The patient presents now a very remarkable picture when we note the contrast with his previous condition. The most successful therapy in this disease is clearly radiation, with radium itself, and not use of the *x*-rays.

POSTURAL ALBUMINURIA

Demonstration of Patient. The Methods of Arriving at a Differential Diagnosis Between Postural Albuminuria and Nephritic Albuminuria. Short Historical Sketch of the Development of Clinical Knowledge of Postural Albuminuria and of the Theories as to its Causation, with Literature.

March 10, 1917.

DR. JANEWAY: The patient we shall see today presents a very important problem, a problem which any of you may be called upon to solve after you begin practice, and which, if you remember this patient, you will undoubtedly solve correctly. If you do not recognize the condition you will make the members of some families desperately unhappy until someome comes in who knows more about it than you do. So I should like you to pay close attention to the facts as Mr. Shipton places them before us.

MR. SHIPTON: The patient, D. H. (Med. No. 37,347), a young boy eighteen years of age, came into the hospital complaining of general weakness, swelling of the ankles, and muscular cramps.

Family History.—Negative.

Personal History.—At the age of three he had diphtheria, followed immediately by scarlet fever, and with both illnesses he had a high fever. He had measles during childhood and recurrent attacks of tonsillitis until his tonsils were removed three years ago. At that time he was to have had a septum operation, but the surgeon's request for a urinary examination before the operation disclosed albumen in the urine, and the operation was postponed until the albumen could be cleared up. The patient was told to watch for swelling of the ankles and the other usual signs. These did not appear until about two weeks ago, when he began to have general weakness. He states that his

ankles swelled and there were vague eye-signs. Three and a half years previously he had been given glasses for the relief of headaches, but he has continued to have occasional throbbing headaches in the temporal region. He came into the hospital because of the albuminuria and the swelling of the ankles.

Dr. Janeway: The history would not seem to admit of any question as to its interpretation. What would it suggest?

Mr. Shipton: I should not like to say merely from the history—but one might think of nephritis.

Dr. Janeway: One might consider the existence of nephritis or of there being some features not evident from the history, or that the history itself as given is not entirely accurate. The patient was sent in with the diagnosis of nephritis, and was studied with this diagnosis in view. What did the physical examination show?

Mr. Shipton: The physical examination, including the examination of the eye-grounds, was negative.

Dr. Janeway: The patient is not a very robust looking boy. He has a deflected septum, a clean tonsillar ring, a somewhat sallow skin color, but fairly red lips. What is the blood-count?

Mr. Shipton: The blood-count is normal, with the exception of the white count, which was 17,600 on admission, with a normal differential. Since admission the white count has been 16,600.

Dr. Janeway: Has anything been found to account for the leukocytosis? There is no eosinophilia; there is a perfectly normal differential count. Has he any antrum or sinus infection that you could discover?

Mr. Shipton: No.

Dr. Janeway: He has an unquestioned leukocytosis with an otherwise normal physical examination. What was his blood-pressure?

Mr. Shipton: The blood-pressure was over 90—between 90 and 100.

Dr. Janeway: The systolic pressure has been steadily just below 100; the diastolic from 60 to 62. This for a boy of eighteen is a subnormal blood-pressure, just the opposite of what we

should expect in a true chronic nephritis. What did the urinary examination show?

MR. SHIPTON: On admission the urine contained a heavy cloud of albumen and an occasional white blood-cell, but no casts.

DR. JANEWAY: The specific gravity was 1011 and the urine was acid, so that from the urine examination we have clear-cut proof of a marked albuminuria in his admission specimen; but from the physical examination there is no evidence of the secondary changes in the cardiovascular system and in the eye-grounds which go with a true nephritis. There was no edema. What impression did you get on cross-questioning the patient as to the reality of the swelling of the ankles?

MR. SHIPTON: The swelling of the ankles and muscular cramps, with vague eye symptoms and ringing in the ears, could not be brought out on cross-questioning. The patient said he could stop the ringing in the ears by putting his fingers in his ears and shaking them. When asked to describe the muscular cramp it became evident that it was not a cramp, but a vague desire to "snap his arm out." In regard to the swelling of the ankles, he had no idea of any time when they were larger than at other times.

DR. JANEWAY: He had never tried to dent his ankles with his fingers. He had been told by his physician to be on the watch for swelling of the ankles, so that we have the possibility of a large element of suggestion. Here I should like to warn you about telling patients of symptoms that may be expected to occur and giving them the responsibility for making the observation. It is a dangerous practice, and in some cases has a very unfortunate effect. Nervous patients will raise heaven and earth to discover the symptoms. It is a delegation of responsibility that no physician should be guilty of. If you feel that symptoms may occur it is your duty to be on the lookout for them yourself, or, in the case of a child, to have a member of the family who can be trusted watch for them; with the insistence, however, that if the symptoms occur you be called in to verify their existence. But when you are dealing with young and impressionable adults, it is better to watch for the symptoms yourself, or do without

them if there is no particular importance to be attached to them. Under no circumstances suggest to the patient things that may happen. Here was a boy with a marked albuminuria and with a low blood-pressure who had been told he had nephritis and was sent into the hospital. What possibilities would suggest themselves to you, Mr. Clark?

MR. CLARK: I think we should consider the amount of albumen in the urine during the entire day.

DR. JANEWAY: You mean that one ought to examine specimens of urine several times a day. You suggest this because you know that there is in young individuals a type of albuminuria which is intermittent and is associated with the posture. Not knowing this, one would not think to examine the urine several times a day. There is a possibility in such a case that the albuminuria is a more or less isolated symptom. In these cases is there usually a considerable albuminuria or only a trace of albumen?

MR. CLARK: There is often a very heavy albuminuria.

DR. JANEWAY: It is the large amount of albumen in the urine which leads to the assumption of nephritis in these cases. What other type of kidney disease is associated with albuminuria, a low blood-pressure, and no cardiovascular or eye-ground changes?

MR. CLARK: None that one would expect to find in a boy of this age, such as amyloid kidney.

DR. JANEWAY: Amyloid kidney has no particular age predilection.

MR. CLARK: It generally follows such chronic diseases as tuberculosis or bone disease.

DR. JANEWAY: It is a secondary renal lesion and, for the diagnosis, there must exist a primary focus of suppuration, chronic tuberculosis, or syphilis. I have seen one very striking case of amyloid disease affecting the kidney and to a slight degree the liver and spleen and the intestine, associated with very large glands of the neck, which we assumed were the primary source of infection, because they were noticed first by the patient, but on sectioning the glands they were themselves found to be the seat of extensive amyloid changes. Dr. MacCallum care-

fully scrutinized every part of the body, but could not find a single focus of disease. The patient had a negative Wassermann. He was in the hospital two months, with the clinical picture of progressive edema, a highly albuminous urine, persistent and almost uncontrollable diarrhea, and occasional intestinal hemorrhage. The causation was never solved; but such cases of unexplained amyloid are very rare. Degenerative renal lesions, which do not give rise to hypertension and cardiovascular changes, we may speak of as nephroses. Not all of them are amyloid. Almost invariably these patients come to us with the clinical picture of an obstinate edema and more or less anemia. They never die a uremic or cardiovascular death, but usually of an intercurrent infection. They run a course of a few months to two or three years, though in rare instances we see cases of this type with periods of latency. We had such a case here under observation, and the patient, I believe, is still doing very well since he had his tonsils removed and his sinuses cleaned out.

Of course in a case of this kind the first problem to solve is as to the existence of a postural albuminuria. Is there anything at all suggestive, Mr. Shipton, in the physical examination?

MR. SHIPTON: He has a striking lordosis.

DR. JANEWAY: Is there any connection between a lordosis of the lumbar spine and postural albuminuria?

MR. SHIPTON: They occur in association very frequently.

DR. JANEWAY: Jehle's name is particularly associated with the relation of lordosis to postural albuminuria. One looks, in these cases, for lordosis of a special type, affecting the upper lumbar spine—according to Jehle the twelfth dorsal and first two lumbar vertebræ—while the more usual type affects the lower lumbar spine.

You will see that this patient, standing in a fairly natural posture, exhibits a rather high degree of lordosis, which is most marked, I should think, at the junction of the second and third lumbar vertebræ, and which apparently also reaches to the twelfth thoracic. He has no limitation of movement whatever in the spine. The greater the effort he makes to stand straight, the further he lordoses his lumbar spine. He is about as hollow-

backed as possible. There is a curious difference between the human and the horse in this connection—this sort of back in a horse would be an evidence of extreme age, while in the human it usually occurs in extreme youth. Of course, the opposite side of the picture (turning the patient) is the one we are more apt to consider, the anterior view, in which the gastro-intestinal specialists are interested, and which they call the *habitus enteroptoticus*, but for the moment we are concerned with the reverse picture.

This one suggestive feature of the physical examination you would not think to look for unless you knew the association of lordosis and postural albuminuria. We test these patients in several ways, depending on our knowledge of what has heretofore been described in relation to this type of albuminuria. To make a diagnosis the patient must first be put to bed for a considerable period, to make sure that the urine becomes free from albumen after a reasonable length of time. We cannot accept the test of the urine from the first hour in bed after considerable standing, because there will be some trace of albumen for a time after assuming the recumbent posture. But the second specimen ought always to be albumen free, or we are not dealing with an uncomplicated case of postural albuminuria. After determining that the urine is free from albumen while the patient is flat on his back, we can have him stand in a markedly lordosed posture against a wall for a period of half an hour to an hour; this will usually produce extreme albuminuria, and on putting the patient back to bed the albumen will promptly disappear. Our patient has been walking and standing for half an hour before coming down to the clinic. We shall have him stand for a short while in the posture I have described; he will then go outside and pass his urine, and we shall see what the tests show, comparing the specimen with the urine passed before he got up at 11.30 this morning.

I want to say a few words about the history of this condition; how it came to be recognized, and how this type of albuminuria was separated from other forms, particularly from true nephritic albuminuria. You know that our knowledge of albuminuria as

a symptom of kidney disease is not yet one hundred years old—or, better, it is a little more than a hundred years old, because there were forerunners of Richard Bright toward the end of the last century. The most important of these was William Charles Wells, an American Tory in England, who made some interesting observations on the relation of albuminuria to renal disease; but the main credit for our knowledge of the importance of albuminuria as a symptom of lesions of the kidney is due to Richard Bright, whose publications appeared from 1827 on. For a long time afterward attention was directed toward the utilization of albuminuria as a means of recognizing renal disease, and more and more the assumption grew that albuminuria was proof of the existence of renal disease. The first cases that were well reported, showing that albuminuria might exist over long periods of time without any proof of renal disease, appeared in a publication by Moxon in Guy's Hospital Reports for 1878. He reported two types, one the so-called "adolescent albuminuria," and one which he called "remittent albuminuria," in which considerable quantities of albumen were found to appear in the urine regularly at certain times of the day—almost always in the morning or some time in the day well after rising—and that the urine passed when these patients first got out of bed was very regularly albumen free. He talked the question over with Sir William Gull, who said he had noticed such cases and had ascribed the condition to atony of the vessels. Immediately after Moxon's publication, Rooke, Binney, and Ferguson each reported cases in the British Medical Journal, and Rooke especially called attention to the regular occurrence of albumen in the morning urine passed when the patient had been up and about, and its disappearance when in bed, and reported a case in which the albuminuria had no relation to renal disease. Leube at that time made a study of 119 soldiers, and in 14 found albumen in the specimens passed in the middle of the day, while the urine was always albumen free in the early morning. He came out strongly for the frequent occurrence of albuminuria in perfectly healthy young individuals under different physiologic conditions. He related it, however, more especially with the effect of exercise than with the effect

of posture. Johnson, who was one of the greatest authorities on renal disease, described intermittent and latent albuminuria, but held that albuminuria always had a pathologic significance, and unless it was due to a temporary discoverable cause and the casue could be removed, the patient must be considered as having true nephritis. He called attention to 3 cases in which he had observed marked albuminuria following cold bathing. I know of a patient who was refused life insurance because he always had casts and a trace of albumen in his urine when examined. He finally came to my father, who did a little detective work, and found that he went for the examination late in the afternoon, and that he was regularly in the habit of boxing in the afternoon and afterward taking a cold shower-bath. My father tested him and found that albumen, with a shower of hyaline casts, appeared in the urine only after a cold bath following violent exercise. The man was seen thirty years afterward, still in perfect health.

The first absolute demonstration of the existence of a type of albuminuria appearing intermittently in young adults and children was given by Pavy, who wrote a group of articles on what he called "cyclical albuminuria," which term still appears in the literature. He did not recognize clearly the importance of posture in relation to these albuminurias, but thought they were dependent sometimes on fatigue, sometimes on exercise, but always on some feature of the diurnal activity. In 1887 Stirling, another English observer, published a paper in which he advocated the use of the term *postural albuminuria*, and showed clearly that the albuminuria was definitely related to the assumption of the upright posture, and that the other influences did not hold for this group of cases.

There have since been a number of publications dealing with this condition. A term which is in very common use is *orthostatic albuminuria*, which was first suggested by Heubner. Later there came to be great interest in the explanation of postural albuminuria, beginning particularly with the publication of Jehle, in which he advocated the view that the albuminuria is invariably associated with a peculiar type of upper lumbar lordosis. He

therefore named it *lordotic albuminuria.* Of course, anyone who advocates an exclusive theory of the origin of a disease must expect to meet with a great deal of criticism and opposition, and this is true of Jehle's theory. Pollitzer has taken the view that in a large number of these cases a subnormal type of constitutional development exists in which the individual cannot maintain the upright posture with perfectly normal physiologic function. He calls this a static neurosis, and states that the albuminuria is not caused by the upright posture, but that the kidneys of these individuals are liable to the development of slight lesions with mild infections. He believes the albuminuria should be considered as of significance, and in many of the cases as dependent on renal lesions, which in those patients who have no static neurosis would be insignificant. This represents a point of view midway between that of Jehle and that of Senator, who believes we should be very skeptical in assuming that the albuminuria is harmless. Heubner, on the other hand, insists that the albuminuria does not signify the existence of any permanent underlying renal disease. There has been a great deal of dispute as to whether lordosis is the essential causative factor—Jehle maintaining that it is; Politzer, that it is not; Heubner, Langstein, and others showing that it is often, but not regularly, present.

Brugge, a Scandinavian, has published a long study of many school children, in which he demonstrates what I think was suspected by most of us before, that lordosis is an important but not an essential factor; that a considerable degree of lordosis may exist without albuminuria, and that the albuminuria may exist without lordosis.

One of Jehle's strong points was that the condition might be produced with the patient in a horizontal position by putting several pillows under his back, so that it ought not to be called orthostatic albuminuria. This has been taken up by a French writer, Jeanneret, who observed the posture of school children at their desks, and who states that those children who sit at their desks in a lordosed position pretty regularly have albuminuria during the school hours, while those who sit in a natural position do not. He has shown a still further element in the rigid main-

tenance of a posture, which explains to a considerable extent why in most of these cases the albuminuria is maximal during simple standing, and is very much less or even disappears entirely during active muscular exercise in the erect posture. Jeanneret holds that there are three elements in the production of the albuminuria: (1) the erect posture; (2) rigid maintenance of the erect posture, with marked contraction of the back muscles; and (3) the lordosis; and that if these three factors can be combined albuminuria will always be produced; further, that where there is a marked pre-existing lordosis it will be brought out very easily. Langstein's article is perhaps the most sensible one. He reports a very interesting case and brings up the question of prognosis. This was a case he observed in Heubner's clinic, which might easily have been reported—if a postmortem examination had not been made—as proving Senator's view that these cases frequently turn out to be cases of true nephritis. The patient was a girl of ten years, who first came to the clinic in March, 1903, with a typical postural albuminuria. The following November she went to an oculist for eye symptoms, and his diagnosis was albuminuric retinitis. She began to have headaches and vomiting, and it was thought she was uremic. She later came back to the clinic, where a diagnosis of brain tumor in a silent area was made, with double choked disk. She went on until 1905, when she died in convulsions. Heubner made a minute microscopic examination of the kidneys and found absolutely no abnormality except the cicatrix of a recent infarct.

(Here the last specimen of urine was shown.)

Dr. Janeway: There is an interesting point in connection with the albumen in the urine of this patient. The majority of nephritics show only albumen coagulable by heat, that is, a true serum protein. This patient also shows a large amount of protein precipitable by acetic acid, which was earlier considered a nucleo-albumen, but which recent workers suggest may be euglobulin. I have seen one urine which on the addition of acetic acid became a perfectly solid jelly in the cold. The specimen we have here contains a large amount of albumen. The previous specimen demonstrated perfectly clearly that there was no

albumen in the urine when he first got up. The urine passed after forty-five minutes' standing shows 4 grams to the liter.

These tests bring out an important point which I am using more and more in the diagnosis between nephritic and postural albuminurias. In convalescent patients with nephritis the first time we get them out of bed the albumen usually reappears in the urine. Where there has been an acute nephritis, and you are watching merely the disappearance of albumen, the patient should be kept at rest as long as possible, even if the albumen only reappears on standing; but in patients with postural albuminuria, who have not had an acute nephritis, exercise helps to make a differentiation. Exercise will frequently fail to produce albuminuria in these cases. So far as my experience goes, a true nephritic albuminuria that is brought out by standing will be brought out even more markedly by active physical exercise.

In the present case we see the large amount of albumen after lordosis in bed in a horizontal position, while the urine after a half-hour of active exercise in various recumbent and sitting postures shows a minimum albuminuria in contrast.

The diagnosis depends upon the performance of these tests, noting the effect of the erect posture; of the recumbent position after a sufficient length of time; the presence of a considerable amount of protein precipitable in the cold by acetic acid in addition to true albumin; when the albuminuria is found in a young individual, whether healthy or more or less neurasthenic, more or less badly nourished, and with more or less definite vasomotor disturbances and usually a subnormal blood-pressure. Many of these individuals are not really healthy, but from the standpoint both of their constitutional and skeletal development are subnormal. The treatment is absolutely the reverse of the treatment of nephritic albuminuria. The treatment of the latter is rest in bed and restricted diet; while the treatment of these cases is correction of posture, invigorating exercise, and a full diet.

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DIABETES ASSOCIATED WITH DISTURBANCES OF THE EXTERNAL SECRETION OF THE PANCREAS IN A SYPHILITIC

Demonstration of Patient and of Studies of Duodenal Contents and Fat and Nitrogen Absorption. Discussion of the Relation of Gross Lesions of the Pancreas to Diabetes, and of the Possible Relation of Syphilis and Diabetes. Short Bibliography of this Phase of Subject.

March 3, 1917.

THE first case presented today, which Mr. Rice will tell us about, brings up a very interesting question of etiology in a disease which we are rarely permitted to consider at all from the standpoint of its causation. I shall confine our consideration today largely to this problem of etiology, for during your third year you have had opportunities to study the ordinary clinical features and the more elaborate pathologic physiology of the disease, with its diagnosis and treatment.

MR. RICE: Patient Mrs. A. B. (Med. No. 37,371), born in Germany twenty years ago; married; has been a seamstress for two years.

Family History.—A sister died of whooping-cough at twelve years of age and an uncle, of cancer, at seventy-two years of age. The family is a large one, and with the exception of the sister mentioned are all living and well. There is no history of kidney disease or diabetes.

Personal History.—The patient had whooping-cough in childhood. At two years of age she had scarlet fever, with no complications. Cardiorespiratory history is negative except for a few night-sweats during childhood. She has had a good appetite all her life and her bowels have been regular. There has been no polyuria. Four years ago she had a number of abscesses on her hips. She has been married three years. Her husband has

cerebral lues. She has had two induced abortions and no children. Her weight two years ago was 150 pounds; last summer she weighed 129 pounds, and on admission, February 18th, 87 pounds. On admission she complained of weakness and loss of weight.

Present Illness.—Two years ago, which was one year after her marriage, the patient was told by her friends that she was jaundiced. There were no symptoms at this time except general weakness. The jaundice continued for ten or twelve weeks; the patient noticed bile in the urine, and during this time lost in weight from 150 to 129 pounds.

Dr. Janeway: Is it perfectly clear that there was no pain at that time?

Mr. Rice: The patient states that there was no abdominal pain at all.

Dr. Janeway: On questioning the patient just now she seems very straightforward about the absence of pain. The attack is recent, and there is no reason to question her statement that she never had severe abdominal pain.

Mr. Rice: She was laid off from her work for a few months, but returned to work again last summer, but says she noticed she tired easily and was very weak. About the first of November she had disturbances of vision, and for a week was unable to see clearly. At this time there were also tingling and numbness of the hands and feet. She had cramps in the legs and a feeling of "giving way"; also nervousness. About Thanksgiving time she was told by her physician that she had sugar in her urine and was given a diet low in carbohydrate. She continued the diet for three weeks, and then, noticing no particular improvement, stopped it. There has been a continued loss of weight, from 129 pounds in September to 87 pounds on admission. She has had a very large appetite. Her bowels have been regular. She says there was no particular thirst and she has had no polyuria.

Dr. Janeway: She has had no pruritus?

Mr. Rice: No pruritus vulvæ.

Dr. Janeway: Her symptoms, then, have been altogether general, with failure of nutrition.

MR. RICE: On *physical examination* she shows recent loss of weight and extreme emaciation. The skin is parched and dry; hair is rather dry. There is a positive von Graefe and her eyes do not converge well. She has some pyorrhea. The tonsils are slightly enlarged. There is slight impairment at the right apex. There is a systolic blow at the apex of the heart. The abdominal examination is negative and shows no tenderness anywhere.

DR. JANEWAY: You found no particular enlargement of the liver?

MR. RICE: The liver, as I remember, came just to the costal margin on palpation.

DR. JANEWAY: The liver comes at least two fingerbreadths below the costal margin and the left lobe is correspondingly enlarged. The liver, however, is not firm, and is very easily pressed away from the abdominal wall, so that it is rather difficult to feel the edge at any point except beyond the border of the right rectus. There is, though, definite enlargement. Is a moderate smooth enlargement of the liver at all common in diabetes?

MR. RICE: I should think it would be where there is emaciation.

DR. JANEWAY: It is fairly common, usually from fatty changes. In this patient one gets no tenderness even on very deep pressure in the epigastrium over the usual site of tenderness for the common bile-duct, nor over the gall-bladder region.

MR. RICE: There is suggestive clubbing of the fingers and toes. The reflexes are normal.

The *blood examination* shows 5,000,000 red cells, 8200 white cells, and 62 per cent. hemoglobin. The differential count is practically normal.

A few days before her admission to the hospital she noticed that her *urine* had changed from a straw color to a dark color, with diminution in quantity. On admission the urine was straw colored. It showed a specific gravity of 1048 and contained a large amount of sugar. The first specimen, unfortunately, was not analyzed quantitatively. There was a trace of albumen.

DR. JANEWAY: What has been the course of the glycosuria?

MR. RICE: The first day the analysis was done she had a slight amount, which cleared up immediately.

DR. JANEWAY: The glycosuria was somewhat over 20 grams the first day on an unknown diet. The second day in the hospital there were only a few grams of sugar in the urine, on what diet?

MR. RICE: On a diet of 1000 calories with low carbohydrate, probably not over 10 grams.

DR. JANEWAY: A so-called carbohydrate-free diet of 1000 calories, and on the second day the urine was practically sugar free. She was not, however, starved at any time. The urine remained sugar free from the third day until the twenty-ninth, when sugar reappeared in the urine in association with certain studies we were making of the integrity of her external pancreatic function. As the case stood at this time what was there about it which would indicate that the patient had anything but an ordinary diabetes of only moderate severity, which was going to do perfectly well on dietetic treatment and on dietetic treatment alone?

MR. RICE: In her stools there was a large amount of undigested meat fiber and fat.

DR. JANEWAY: Much of the fat being neutral fat?

MR. RICE: Yes, it was mostly neutral fat.

DR. JANEWAY: Of course during all this period she was on a comparatively low fat intake and a total restricted diet for the control of her glycosuria. How did the stools remain during this period of four weeks?

MR. RICE: They showed an abnormal amount of fat.

DR. JANEWAY: Even on a fat intake of about 100 grams—she was run up to not over 100 grams of fat—there was constantly present more or less fat. How many stools a day did she have?

MR. RICE: No more than two or three.

DR. JANEWAY: During that period the stools were, as a rule, two a day. On questioning the patient as to whether she has had any intestinal upsets or marked diarrhea, she says that she has never had anything of that sort. When I asked if she noticed before coming to the hospital whether she had large

stools and what they looked like, she states that she has noticed very large stools, and that sometimes there seemed to be big pieces of fat in them, and that sometimes this fat "would run out of itself." She says it was yellow and very similar to oil or butter. I have tried to get this information without suggestion, and, although she has been talked to a great deal about it, I think the information is practically spontaneous. The significant fact is that when cross-questioned she says that at times during the few weeks preceding her admission she noticed that the passages were very bulky and also noticed the appearance of the fat, like oil or butter, which came away of itself. This history is always of great significance and ought never to be neglected. Usually, however, it is not obtained unless inquired for. When Mrs. B. came into the hospital from the dispensary, where I first saw her, there was no suspicion in the minds of any of us that she had anything more than an ordinary diabetes of moderate severity, with an etiology of a very different nature from that which has been considered since Mr. Rice's observations on the considerable quantity of neutral fat and undigested muscle-fiber in the stools. That history, Mr. Rice, always suggests a lesion of what nature?

MR. RICE: A lesion of the pancreas.

DR. JANEWAY: What kind of a lesion?

MR. RICE: An insufficiency, particularly of the ferments.

DR. JANEWAY: But that is not a lesion, is it?

MR. RICE: A pancreatitis or a fibrosis, sclerosis, or calculus or a luetic lesion.

DR. JANEWAY: These are only details. What is the essence of the lesion one would assume in such a case and set out to prove or disprove?

MR. RICE: Insufficiency of the pancreatic juice.

DR. JANEWAY: I think the essence of the lesion is some interference with the flow of the pancreatic juice into the bowel or a lesion so totally destructive as to cause a complete or almost complete disappearance of the external secretion. The important fact is that bulky stools containing large quantities of neutral fat were passed, and that the stools at times looked like butter

or pure liquid fat, with, in addition, undigested muscle-fibers, which always suggests the absence of external secretion of the pancreas from the duodenum; so that we will think back from this to a more detailed diagnosis.

We have at the present time methods for detecting pancreatic ferments either in the stools or in the duodenal contents, and in a case such as the one before us we are not satisfied with the crude assumption, but set out to test for the presence or absence of pancreatic ferments. The first tests were made on the feces. What was found in the feces?

MR. RICE: The pancreatic function test of the feces showed that there were only 15,000 units of pancreatic ferment—that is, of diastase—while the normal amount runs from 60,000 to 240,000.

DR. JANEWAY: There was not quite a complete absence of the diastatic ferment in the stools. Is the pancreas the only possible source of diastatic ferment in the stools?

MR. RICE: The saliva may also be a source.

DR. JANEWAY: If the stomach contents are not so highly acid as to destroy it. No other tests were made in the stools because it is more satisfactory to examine for the ferments in the duodenal contents. What did these show?

MR. RICE: The duodenal contents showed a diminution in the free ferments.

Analysis of Duodenal Contents

Diastase—2 c.c. of 0.1 dilution of duodenal contents reduces 1 c.c. of a 1 per cent. starch solution.

Lipase—1 c.c. of duodenal contents changes neutral ethyl butyrate to a faintly acid reaction, but a measurable amount of acid was not formed.

Trypsin—Metz tube shows less than 1 mm. digestion at end of forty-eight hours.

DR. JANEWAY: Dr. Brown has made a special study of this, using casein, and there was very slight digestion of casein. Were diastase and lipase present?

MR. RICE: Diastase was present in very small amount. Lipase could just be detected.

DR. JANEWAY: Testing with ethyl butyrate gave rise to very slight splitting, so that the evidence from the duodenal contents showed a marked diminution in the amount of pancreatic ferments of all three kinds. What was the clear evidence that you had duodenal contents?

MR. RICE: The patient was given milk when the stomach-tube was in place, and this was not recovered when the tube was drawn back into the stomach.

DR. JANEWAY: Did you obtain bile-tinged contents?

MR. RICE: I do not know whether tests were made for bile, but the contents were slightly greenish.

DR. JANEWAY: Then bile was present. Were they acid or alkaline in reaction?

MR. RICE: Alkaline.

DR. JANEWAY: This shows we are not dealing with stomach contents. The evidence is pretty clear, though perhaps not as clear as we should wish, because a complete absence of ferments is much more satisfactory in making a diagnosis of an organic disease of the pancreas with loss of external secreting function. The loss of the patient's external pancreatic function has been tested in another way, and that is by altering her diet. This was begun on her twenty-ninth day in the hospital. What element of the diet was pushed up?

MR. RICE: The fat was increased gradually in the course of two or three days to about 340 grams a day.

DR. JANEWAY: What was the result upon the stools?

MR. RICE: The stools were large. Their number was not excessive—she still passed only two or three a day—but they contained a large amount of neutral fat.

DR. JANEWAY (specimen shown): I have here a specimen of the stool with this diet. It evidently contains a great deal of perfectly free butter-fat or oil, I don't know which, though it looks like rather yellow butter-fat. Was there any change in the urine coincident with the high fat feeding?

MR. RICE: Sugar began to appear in the urine.

DR. JANEWAY: Was there any other finding in the urine that had not been noticed before?

MR. RICE: She had at one time a little diacetic acid.

DR. JANEWAY: There was no appearance of any considerable acidosis. Is it possible that the glycosuria could have been produced by excessive fat feeding, if fat was not absorbed in sufficient amount to give rise to acidosis or to a marked increase in her ketonuria.

MR. RICE: I should think it quite possible. When a patient takes 20 grams of carbohydrate it would require a great deal of fat.

DR. JANEWAY: The glycosuria ran up to 40 grams on the high fat feeding, but coincident with this she has not developed any diacetic acid in the urine.

(The patient at this point spoke with Dr. Janeway.)

DR. JANEWAY: I have just had an interesting piece of information given me confidentially, which brings out a really important point, a point that all of you who care for diabetics will soon learn from sad experience. There are several things you will have to cut your eye-teeth on in taking care of diabetics—one of these is that a patient who has been doing well on a carbohydrate-free diet, and who comes to you with a urine containing considerable sugar and which does not contain acetone and diacetic acid, may be considered as suppressing facts in regard to the diet. We are not yet at the bottom of the problem of the relation of the fat intake to glycosuria. The fundamental facts given to us by the best students of animal nutrition are that there is as yet no clear evidence that fat is ever transformed into dextrose in the animal organism or in the human organism. The only evidence of the transformation of fat into dextrose has been indirect, gained from the observation of cases of human diabetes of maximum severity, in which the D : N ratio has been increased on an increase of fat in the diet beyond 3.65 : 1, and those cases I think can none of them stand the test of rigid criticism.

The other line of argument has been furnished by the results of Allen's experiments on dogs with partial excision of the pancreas, and from his experiments on human beings, which have

been the basis of his present starvation treatment, which we have all adopted in one form or another. But the evidence here, as I have said, is entirely indirect. It is to the effect that if we reduce the carbohydrate and protein without reducing the fat, in certain patients we may find that the glucose in the urine persists and does not disappear until the fat in the diet has also been greatly reduced. There has been a tendency to connect the fat in the diet directly with the sugar in the urine, which has no definite basis in our present knowledge. Indeed, it is perfectly possible to bring out sugar in the urine of patients whom you have rendered sugar free by the fasting treatment merely by a considerable increase of the fat in the diet, but I have yet personally to find such a case in the literature, or to see a straightforward case myself where such a thing has occurred without the appearance of the acid bodies in the urine. There is a great deal in our recent as well as in our past experience to suggest that acidosis in itself—real acidosis, definite impairment of the alkali reserve of the blood—tends to increase hyperglycemia and glycosuria. This is a relation which I think we can affirm. That such an increase in sugar occurred without the appearance even of diacetic acid in the urine would seem to me *a priori* to point to a break in the observations rather than to a confirmation of the production of sugar from fat. In this case I have in my possession information—perfectly confidential, the source and nature of which, like some of the recent important diplomatic documents, I cannot wholly reveal at the moment—from which the reason for the reappearance of the glycosuria can be very easily unraveled. (The patient confessed to smuggling fruit and other foods into the ward.)

Have any experiments been made, Mr. Rice, in regard to supplying artificial pancreatic juice?

Mr. Rice: The patient has been given raw pancreas and pancreatic extracts with calcium carbonate and sodium bicarbonate for four days. Two days before she was given the pancreatic treatment control observations were made.

Dr. Janeway: Dr. Mosenthal has had the fat and nitrogen of the feces determined during the two control days and the

subsequent period of administration of pancreas. What have the results been thus far?

MR. RICE: On a diet which was kept approximately constant at 340 grams of fat a day, in ten daily stools there was a loss of 94 grams a day, equivalent to 27.5 per cent. of the fat eaten, and the loss of nitrogen was 2.5 grams, or 14.4 per cent.

DR. JANEWAY: What was the effect on this of the subsequent pancreas feeding?

MR. RICE: Just the opposite from what one would expect. The loss of fat increased to 163 grams, or about 50 per cent.; the loss of nitrogen to 5.3 grams, or 32 per cent.

DR. JANEWAY: So far, then, the therapeutic test has given no favorable result, but has yielded strong confirmatory evidence of the correctness of the diagnosis. Unfortunately, our patient has been far from co-operative, and the experiment is anything but a satisfactory one. However, is not 340 grams of fat daily an extraordinary intake to expect a patient to utilize? May not part of the trouble be a failure of the absorptive mechanism rather than of the fat-splitting ferment? Whichever it be, the disturbance of fat utilization is evidently a grave one, and indicates very clearly that we are dealing with a different condition from ordinary diabetes. Du Bois, studying the fat lost by the stools in typhoid fever patients, was able to give one patient more than 300 grams, with a loss of only 5 per cent., and a number of other patients well over 200 grams, with losses between 3.5 and 11.2 per cent., and has made clear what von Noorden pointed out previously, that the more fat given, the smaller the percentage of loss in normal individuals. There are two points which I think we should definitely determine in this case. It is not a clear case as it stands. In the first instance we have breaks in the diet. In the second place we have been asking of the patient supernormal function while we have been trying to replace a damaged function by administering pancreas preparations. Our treatment, you will realize, is very expensive; 163 grams of fat in the feces at the present moment would make a German's hair stand on end. I think the patient should be put on a fat intake of not over 150 grams and the pancreas preparations continued.

If on this treatment she comes down to a 10 per cent. loss we can assume pretty definitely that the pancreas preparation has been of benefit. If we omit the pancreas preparation for two days and then resume it, we shall have a clean-cut test of its efficacy. We are not by this test arriving at a diagnosis, for the results of pancreas substitution in any case are not as brilliant as one would expect. I have had failures with all the dried pancreas preparations, but have observed rather striking success with the use of chopped raw pancreas, served with a little mayonnaise as a salad with each meal. You must be sure, however, that you are giving pancreas. I had the experience in a New York hospital of giving supposed pancreas without result, and a little scrutiny of the material, which was obtained from the butcher's ice-box, showed that the nurse had been giving thymus gland and not pancreas!

Just a word about the bearing of the case. We will take up the question of treatment later. We are here clearly dealing with a patient in whom there is loss of both external and internal secretions of the pancreas. These cases are very rare and are of great importance historically and theoretically. The first observation of such a case was in 1788 by Thomas Crawley, an Englishman, and it is interesting that in practically every disease the first clinical observation has come from the English. The French observed cases, and Lanceraux classified them as "diabète maigre." It was from the known existence of these cases that Minkowski and von Mering were led to make their experiments on pancreas excision, and from them comes our modern knowledge of the relation of the pancreas to diabetes. Hansemann in 1894 collected a large series of cases of diabetes showing pancreas lesions; out of 72, 14 were cases of stone in the pancreatic duct, with more or less complete atrophy of the pancreas. The next important step was the study of the histologic changes in the pancreas and in the islands of Langerhans by Opie. Heiberg's quantitative studies have strengthened the belief that the islands are the source of the internal secretion. Cecil in 1909 collected a series of 90 autopsies and gave a good review of the histologic changes.

The great majority of the cases with loss of external secretion

have been cases of stone in the pancreatic duct, with atrophy of the pancreas so complete that there has been a loss of the islands of Langerhans as well. Mere ligature of the pancreatic duct does not produce diabetes. For the most part it is cases of duct occlusion which have coincident infection running up into the gland and producing interlobular and interacinar pancreatitis that have lost their internal secretion and developed diabetes.

There is another question which arises in the present case. The patient's husband has cerebral syphilis. The onset of her disease was a year after her marriage, and she gives a strong positive Wassermann reaction. When I sent her into the hospital from the dispensary, with no knowledge of the loss of external pancreatic function, it was with the hope that we might treat her underlying lues, and that she might prove to be one of the extremely rare cases of diabetes which have been successfully treated by antisyphilitic therapy. Such a case has been reported by Umber. Joslin has never seen successful results in such a case. I have never seen successful treatment of diabetes by salvarsan.

The question arises, Is there any relation between this patient's loss of external pancreatic function and her lues, or have we to do with the ordinary type of stone in the pancreatic duct and a diffuse interacinar as well as interlobular pancreatitis following infection?

The evidence is very hard to satisfy oneself about. There is a history of painless jaundice. The one essential feature of pancreatic calculus is colic of as severe a nature as with gallstones. This is entirely absent here. We must, I think, leave the question open. I can find no clean-cut case of extensive syphilitic disease affecting the pancreas involving external as well as internal secretion. We are gaining some new standpoints in regard to the relation of syphilis to the pancreas, which, however, I find it very difficult to subject to critical judgment. Warthin, in this country, is making an exhaustive study of spirochetes in the pancreas, in which he finds them frequently associated with many different lesions or with no lesion at all. Umber has observed one straightforward case of diabetes with

disturbance of fat utilization and a pancreatic tumor in a syphilitic. In this case, however, there was a curious story. On the day the patient received his salvarsan he felt "something give way" in his epigastrium. Improvement in his carbohydrate tolerance and fat absorption followed, leading to a final complete cure. I cannot feel that the relation of the syphilis is in any way proved, but prefer to consider his case as one of the diabetes associated with obstruction of the pancreatic duct by a calculus, the passage of which was the cause of the cure.

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CLINIC OF DR. LEWELLYS F. BARKER

JOHNS HOPKINS HOSPITAL

MENINGITIS OF UNKNOWN ETIOLOGY, PROBABLY MENINGOCOCCAL

February 13, 1917.

THE case before us this morning is a very interesting one from the standpoint of etiology, for, though the patient undoubtedly has meningitis, we have thus far been unable to find any bacteriologic evidence bearing upon the diagnosis, and we are, therefore, somewhat uncertain as to the origin of the inflammation. That we have not yet succeeded in demonstrating the presence of the meningococcus in the cerebrospinal fluid in this particular case need not deter us, however, from giving the patient the benefit of the serum treatment. I must agree with Netter, who thinks that the antimeningococcic serum should always be given when there is any suspicion of meningococcic meningitis, without waiting for a positive diagnosis based upon bacteriologic study of the fluid obtained by lumbar puncture. Meningococcic meningitis, as Sir William Osler has said, has the unique and fortunate distinction of being the only form of meningitis in which recovery takes place after treatment in 50 to 70 per cent. of the cases. We have the further satisfaction of knowing that we need never despair of any case, no matter how desperate it may seem, as long as the serum can be administered without loss of time.

Dr. Gardner Robb, of Belfast, has recently reported the case of a young man who one night in February, 1915, went to bed in excellent health, and the next morning was unable to rise on account of intense headache. He soon became delirious, and when seen by Dr. Robb in consultation, fifteen or sixteen hours

after the onset of his illness, he was quite unconscious. His pulse could not be counted at the wrist, there was great rigidity of the neck, and he was covered with a plentiful petechial eruption. There were also several small subconjunctival hemorrhages. The patient's only chance seemed to lie in sending him to a hospital, but Dr. Robb, as well as the medical man who had called him in consultation, felt very doubtful whether he would survive the necessary journey of four or five miles. It was the only hope, however, and they sent him in. He was still living when he reached the hospital, and a lumbar puncture was made as soon as he arrived, a purulent fluid being withdrawn in which meningococci were plentiful, both intra- and extracellular. Forty c.c. of the Flexner serum were injected and twelve hours later another dose of 20 c.c. was given. At this time the patient seemed no better, and the whole cornea of one eye was "steamy" with pus in the anterior chamber. Injections of serum were given each day for several days and he slowly improved, until, at the end of ten weeks, he was able to leave the hospital, entirely recovered, save for the loss of one eye. In the autumn of the same year he was heard from as well and hearty and earning his living as a carpenter at a munitions factory.

As Dr. Robb truly remarks, "if this patient had died, he might readily have been put into the category of cases that were 'hopeless from the first.' "

The patient I am presenting to you today is a young colored girl, Elizabeth S., sixteen years old, employed as a nursemaid. She came to the Gynecologic Dispensary on January 25th, complaining of pain in the left side of the back, extending down the left leg, which had begun on January 20th, five days previously. Two days before she came to the dispensary she began to have a slight cough. Examination in the gynecologic department was negative, and she was sent to the orthopedic service. When seen by the orthopedists on January 31st, six days later, she said the pain had extended to the lower ribs on the left side and also to the region over the ilium. She complained of chills and sweats, and also of nausea and vomiting. Her temperature was

then 102° F. Examination by the orthopedists was also negative as far as the bones and joints were concerned and she was advised to enter the hospital, which she did on the same day, January 31st.

Listen attentively to this history. The patient complained of pain in the left side of the back, extending down the left leg, when first seen in the gynecologic department, but when seen in the orthopedic department, six days later, she said she had chills followed by sweats, as well as nausea and vomiting. Her temperature was 102° F. When admitted to the hospital the same day, she said the pain was in both hips. This localization of the pain in the hips sounds as if the case might possibly be one of arthritis of the hip-joints.

On questioning her regarding her family, we learn that there is, among its members, no history of tuberculosis nor of disease of the heart or of the kidneys. The patient herself had measles as a child, but otherwise her past history is negative.

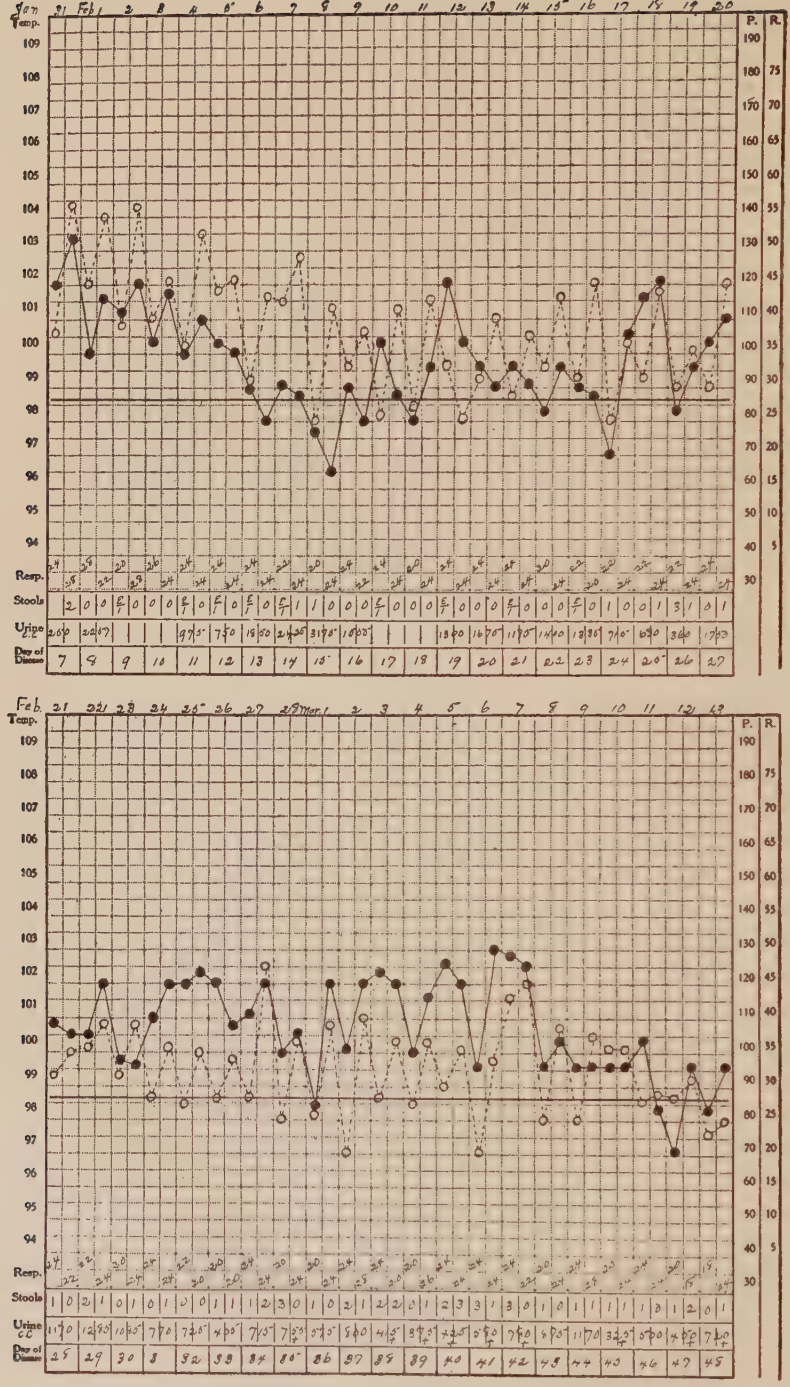
Physical examination on admission showed a well-nourished, well-developed, light mulatto girl. Her face was slightly flushed. There was no jaundice and the mucous membranes were of a fairly good color. Her mind was clear. Examination of the head was practically negative. It is well formed and there are no exostoses. The pupils were equal and reacted normally to light and to accommodation. The extra-ocular movements were normal and there was no strabismus. The throat and nose seemed normal except that there was some slight impediment to nasal breathing. Were her nose and throat examined by a specialist?

STUDENT: No. The interne said that, on inspection, they looked normal.

DR. BARKER: It is desirable to have an examination of the nose and throat by a specialist in a case of this kind. I would have you note that she has had a cough which began four days after the onset of her illness. Was there any sign of herpes?

STUDENT: No.

DR. BARKER: Herpes is a very common accompaniment of meningococcal meningitis. The genito-urinary and neuro-


Jan. 31 Feb. 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Temp.
P.
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Feb. 21 22 23 24 25 26 27 28 Mar. 1 2 3 4 5 6 7 8 9 10 11 12 13
Temp.
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50 Fig. 4.—Temperature chart showing type of fever in text case.

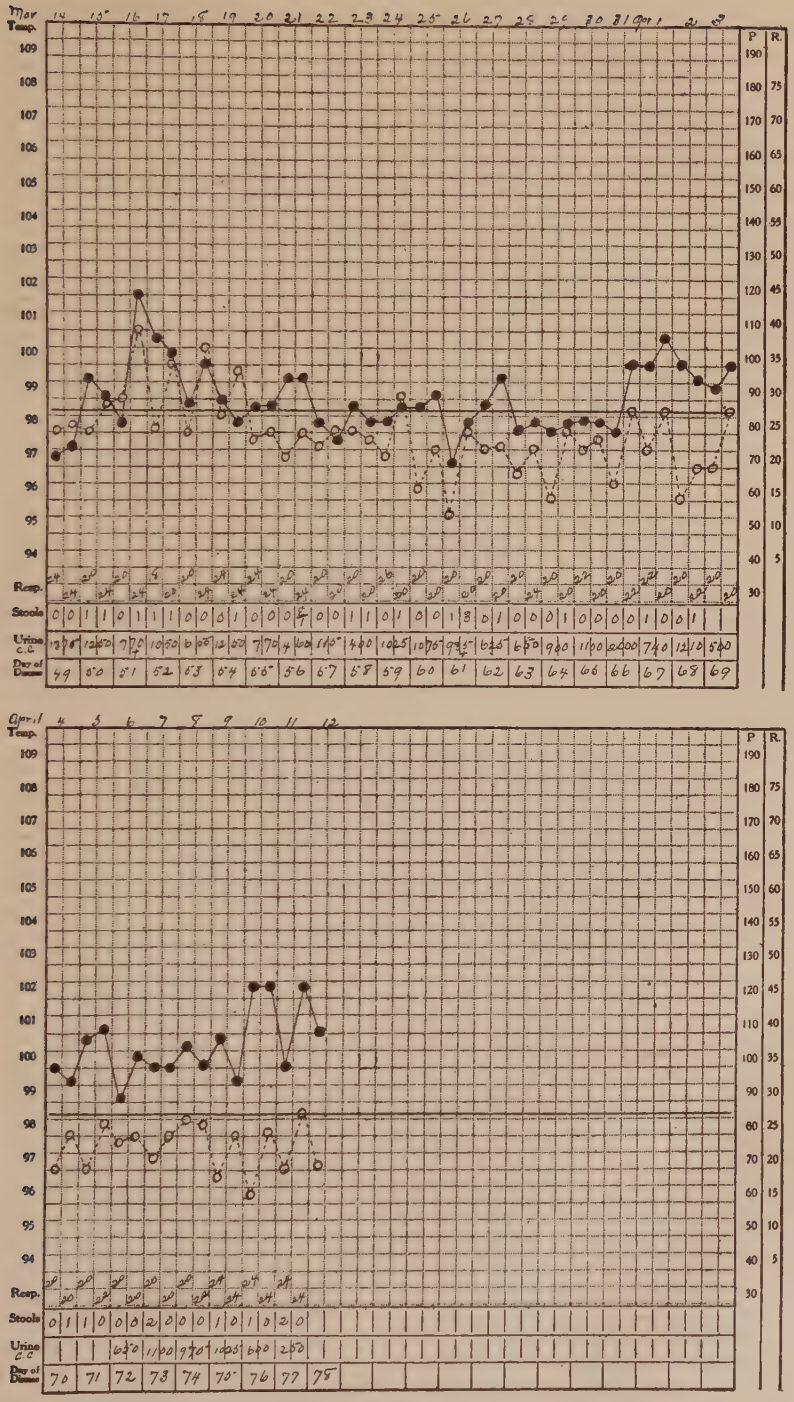

Fig. 5.—Temperature chart showing type of fever in text case.

muscular systems were negative. There was no hemiplegia or paraplegia. The gastro-intestinal tract was normal except for the fact that she has had some diarrhea for the past two years to the extent of four stools daily. This decreased to two stools a day at the beginning of her present illness. The cervical glands at the angle of the jaw are slightly enlarged, but there is no general glandular enlargement. There was no mastoid tenderness.

The tongue was protruded in the median line; it showed a slight tremor. The tip and edges were red and the rest of the tongue was heavily coated. The pharynx was slightly injected and there was a slight exudate on the tonsils. The neck was not stiff at the time of admission, but there was slight tenderness on deep pressure over the cervical spine. The thorax was practically normal except that the percussion note was slightly impaired below the left clavicle in front, with bronchovesicular breathing in the same region. Over the back there was an increase in the whispered voice and the breath sounds. An *x*-ray examination of the lungs showed infiltration beneath both clavicles and clouding of the apices. The record of the examination is accompanied by the note that Dr. F. H. Baetjer regarded these changes as tuberculous in nature. Examination of the spine showed some tenderness over the lower sacral region, especially marked on change of position. The heart was normal. The abdomen was slightly fuller than normal, but there was no tenderness or muscular rigidity. The spleen could be felt one or two finger-breadths below the costal margin. Make a note of the fact that the spleen was palpable. It is an important point. Was it soft or hard?

STUDENT: Soft.

DR. BARKER: Softening and enlargement of the spleen generally indicate some form of acute infection. There was pain over the sacro-iliac region, but movement of the legs was not restricted. The knee-jerks and the ankle-jerks were sluggish on both sides. Note that the reflexes were sluggish, for it is an important point. How about the Babinski sign? That also is important.

STUDENT: It was negative and so was Oppenheim's sign.

DR. BARKER: How about the abdominal reflexes?

STUDENT: They were present.

DR. BARKER: The blood examination showed:

R. B. C., 4,216,000.
W. B. C., 4350.
P. M. N., 44 per cent.
P. M. L., 1 per cent.
P. M. B., 0 per cent.
L. M., 30 per cent.
S. M., 24 per cent.
Trans., 1 per cent.
Hb., 60 per cent.

Notice that we have here a moderate anemia with low color-index and a leukopenia at the beginning of the illness. The leukopenia, together with fever and a palpable spleen, suggested the possibility of either typhoid fever or malaria. There were, however, no malarial parasites in the blood. Was a good search made for them?

STUDENT: Yes.

DR. BARKER: The Widal test was negative and the Wassermann test was also negative. Were any blood-cultures made?

STUDENT: Yes.

DR. BARKER: At what date?

STUDENT: On the night of admission; they were negative.

DR. BARKER: When a diagnosis is not clear in a patient with a high temperature a blood-culture should always be made. Many a time it saves us from a bad mistake. In the first week of typhoid fever the blood-culture is positive in 90 per cent. of cases. The same is true of lobar pneumonia; you can grow the pneumococcus from the blood within twenty to twenty-four hours in a large proportion of cases. In acute meningitis you may get in a blood-culture the meningococcus, or some one of the other organisms that cause the disease, in one-third of the cases within twenty-four hours. This point is so valuable that I cannot emphasize too strongly the importance of taking a blood-culture within twenty-four hours in every patient with an outspoken fever. As a medium for the blood-cultures it is well

to use (1) blood-agar, (2) bile-bouillon, and (3) Rosenow's graded oxygen medium.

On the night of the patient s admission there was a positive Kernig sign, and as it was present, a lumbar puncture was made next day. This was a wise procedure. The presence of Kernig's sign with pain in the back and rigidity of the neck are definite indications for lumbar puncture. The spinal fluid removed was bloody, but that may have been due to injury by the exploratory needle, which cannot always be avoided. Sometimes one hits a minute blood-vessel and the result is a bloody fluid. The presence of blood vitiates the cell count of the cerebrospinal fluid, of course, but a culture can be made. The little hemorrhage interferes with the cytodiagnosis, but not with the bacteriodiagnosis. Another leukocyte count was made after the lumbar puncture, and showed 7600 white blood-corpuscles.

The lumbar puncture was followed by nausea and vomiting, but the patient became comfortable again within a short time. Nausea and vomiting are not uncommon after lumbar puncture, and patients sometimes have headache as well; in this case, however, the patient had had nausea and vomiting previously, doubtless due to the meningitis itself.

Next day one rose spot was seen on the abdomen. Remember that it is necessary to be very cautious in drawing inferences from the finding of a single rose spot. Unless rose spots occur in crops, it is wise not to lay great stress upon them as a diagnostic sign. A rose spot is, nevertheless, so characteristic that it is not likely that a skilled observer will make a mistake in regard to its nature, but you should remember that rose spots occur in more than one disease. The commonest of all conditions under which they are found is typhoid fever, but they may also be present in typhus fever and in meningitis, as well as in some other diseases. On February 8th the patient complained of stiffness of the neck and the abdomen was somewhat more distended. Kernig's sign continued to be positive.

A second lumbar puncture was made on February 8th, and a small amount (15 c.c.) of turbid, colorless fluid, which was under slightly increased pressure, was withdrawn. A cell count

showed 1800 cells per cubic millimeter in the fluid; the majority of these cells were polymorphonuclears, though along with them a moderate number of mononuclears could be observed. The Ross-Jones sign was positive. Were there any fibrin masses in the spinal fluid?

STUDENT: No.

DR. BARKER: Note that the fluid was turbid and the cell count was high. Such a finding almost always indicates what?

STUDENT: Meningitis.

DR. BARKER: Yes, but it indicates something more. Turbid spinal fluid with a high cell count signifies *leptomeningitis*, and, more than that, it signifies *acute leptomeningitis*, and, still more, it means *acute purulent leptomeningitis*. The presence of tubercle bacilli in the fluid would indicate tuberculous meningitis. Were any tubercle bacilli found?

STUDENT: No.

DR. BARKER: How was the fluid examined?

STUDENT: It was centrifugalized and the centrifugate was stained with methylene-blue. Other preparations were especially stained by the Ziehl-Neelsen method for demonstrating tubercle bacilli.

DR. BARKER: Were no cocci nor influenza bacilli visible?

STUDENT: No.

DR. BARKER: The examination of the stained smears was, as you see, somewhat disappointing. One should look through a large number of fields, and if no bacteria are found, several smears should be made and a thorough search made. I recall a case I saw in consultation with Dr. Frank Martin at St. Joseph's Hospital. Several smears had been examined with negative results, but we made still another smear, and to our gratification finally ran across a cell the protoplasm of which was closely crowded with meningococci. In the same smear we found a few other cocci both intra- and extracellular. Had we stopped short of this final smear we should have failed to find the cocci!

When you get a purulent fluid, you should be sure to make a culture on some medium that can be relied upon to grow the organisms that are found in cases of meningitis.

Was a culture made from the cerebrospinal fluid of this patient?

STUDENT: Yes; at the time of lumbar puncture.

DR. BARKER: What medium was employed?

STUDENT: I don't know.

DR. BARKER: Probably blood-agar was used. I think that is the medium that our clinical bacteriologist, Dr. Sydenstricker, finds best. Most of the organisms likely to be present in meningitis will grow upon blood-agar; the meningococcus, the pneumococcus, the streptococcus, and the influenza bacillus would all be "caught" by that method of culture.

After the second lumbar puncture the patient complained of severe pain in the lumbar region, radiating down the left thigh. I would have you notice, however, that the first symptom in this case was pain in the left side of the back and around the left hip, extending down the left leg, and it was on account of these pains that the patient was referred to the orthopedic department.

The blood-culture was again negative about this time. Here we have two negative results as regards the blood-culture. A third lumbar puncture was made on February 12th, four days after the second. The fluid withdrawn was turbid and contained 900 cells per cubic millimeter, the majority of them being polymorphonuclears, though a good many lymphocytes were also present. The Ross-Jones sign was still positive. The presence of globulin is not very important for differential diagnosis here, but the presence of a large number of polymorphonuclear cells is. In tuberculous meningitis the cells present in the spinal fluid are, as a rule, largely nononuclears, whereas in the non-tuberculous purulent forms the polymorphonuclears are largely in excess. The presence of a large number of polymorphonuclears is, as far as it goes, in favor of purulent meningitis of non-tuberculous origin, but it does not go far; in fact, it is, in reality, of little differential diagnostic value, for although the lymphocytes are usually in excess in tuberculous meningitis, there are, notwithstanding, quite a number of tuberculous cases in which the polymorphonuclear cells exceed the lymphocytes in the fluid obtained by lumbar puncture. In short, though an excess of lymphocytes

speaks for tuberculosis, and it is well to consider that sign in differential diagnosis, it does not do to rely upon it. The presence of pus-cells proves an acute leptomeningitis, but it does not establish its etiology, and unless you can demonstrate the presence of the meningococcus, the streptococcus, the pneumococcus, or the influenza bacillus, or unless the signs are sufficiently marked to make the diagnosis in themselves, I advise you to leave the etiologic diagnosis open. In this case it is very important to know the nature of the organism concerned because of the treatment. The Wassermann reaction, you say, was negative?

STUDENT: Yes; negative. We felt that we could rule out lues.

DR. BARKER: Sometimes meningitis is secondary to a primary focus of infection in the ears, or in the nose and throat. Have the nose, throat, and ears been examined in this case by a specialist?

STUDENT: No; not yet.

DR. BARKER: In a case of this kind we may have to deal with a meningococcus infection or with meningitis associated with some acute infection like typhoid fever, lung abscess, empyema, or pelvic infection. Or we may be dealing with a rhinoleptomeningitis secondary to trouble in the nose; or, what is more common, with an otoleptomeningitis secondary to suppuration in the ear; or, rarest of all, with an ophthalmoleptomeningitis, where an acute infection of the eye extends backward. But there is no evidence in this case of a rhinogenous, of an otogenous, or of an ophthalmogenous origin. Let us consider the course of the illness in the hospital. What was the disease thought to be on admission?

STUDENT: The impression on admission was that the patient might have typhoid fever.

DR. BARKER: Yes. The leukopenia, the palpable spleen, the distended abdomen, and the possible rose spots, all were suggestive of typhoid. Meningitis and meningismus were thought of, however, from the beginning, on account of the positive Kernig sign. Moreover, either meningitis or meningismus may occur as a complication of typhoid. In primary men-

ingitis we very often observe, from the beginning, rigidity of the neck and retraction of the head, with severe headache and hyperesthesia of the skin, as well as Kernig's sign. The Widal test, however, in this case was negative. I think we may rule out typhoid, but not on account of the negative Widal reaction, for it is not worth anything as a diagnostic sign in the first week or ten days of the disease. Indeed, the Widal reaction may never be positive at all throughout the whole course of a typhoid infection, and when it is positive, it is usually only after the disease has existed for some time. It was right to make the test because the patient might have come in late in the course of a mild typhoid infection the nature of which had been overlooked.

Negative blood-cultures early in a febrile disease are strongly against the diagnosis of typhoid, though they do not rule it out entirely. In this instance we have two negative blood-cultures, and the negative results are important as showing the absence, at any rate at the moment when the blood-cultures were made, of a bacteremia. Lues is ruled out because of the negative Wassermann reaction. One of the students has asked me whether we should not consider the possibility of uremia. How about albuminuria?

STUDENT: There was a slight amount of albumin in the urine.

DR. BARKER: Were there any casts in the urine?

STUDENT: No.

DR. BARKER: I think we may rule out uremia, not only because the urinary findings are only those of a slight toxic nephropathy, but mainly because of the symptoms of meningeal irritation and of the positive findings in the cerebrospinal fluid. The anatomic diagnosis of an acute purulent leptomeningitis is here certain; our real difficulty lies in the making of an etiologic diagnosis. Before discussing the etiology further, however, let us ascertain the present condition of the patient. She is, as you see, a mulatto girl, about sixteen years old. There is no history of tuberculosis in her family and she shows no signs of tuberculosis except this slight dulness below the clavicle and the increased vocal sounds on the left. The *x*-ray, however, as you have heard, and as you see in this plate, shows definite infiltration

of the left upper lobe and this roentgenographic picture is very suggestive of a tuberculous process.

There are no signs of herpes at present. (To patient): Does your head ache?

PATIENT: No.

DR. BARKER: Her tongue is heavily coated and red at the tip and edges. It might be a typhoid tongue. The retrocervical glands are not enlarged. She has a burn on her abdomen. What caused it?

STUDENT: A hot-water bag.

DR. BARKER: Burns occur sometimes from hot-water bags, but we do not like to have them occur. Our nurses are very careful. There is not much risk, either, of such an accident with a patient whose psyche is clear, but in a semiconscious patient, especially after an operation, a hot-water bag, if too hot, can do a great deal of harm. I know of one instance, in a very good hospital, in which the bag was filled with water that was too hot, and in addition it ruptured in the bed of a patient recovering from an anesthetic. The result was a very extensive burn. Case settled out of court!

(To patient): Will you please take a deep breath. Now another. The spleen is not easy to palpate now. (To patient): Does it hurt you when I lift your left leg? (*Flexes the thigh, but leaves the leg also flexed.*)

PATIENT: It doesn't hurt me when it is lifted in that way, but it hurts me to stretch it out straight. (*Now extends the leg, while the thigh is flexed at a right angle.*) Oh! That hurts!

DR. BARKER: Now we will try the right leg. Does that hurt you?

PATIENT: Yes.

DR. BARKER: You see that Kernig's sign is positive in both legs. Now we will try for the Brudzinski sign. This, when it is present, is strong presumptive evidence of meningitis of some kind. The patient lies flat on the back, and you flex the chin upon the chest with one hand, while you steady the patient with the other. When the sign is positive the arms are drawn up and the thighs and legs are flexed. It is known as the "frog sign"

because in children, in whom it may be especially well marked in meningitis, the movement of the extremities gives the child an appearance somewhat like that of a frog. The sign is not present here. Another of Brudzinski's signs is known as the "identical reflex." When it is positive the eliciting of Kernig's sign in one lower extremity causes a reflex flexion of the thigh on the opposite side of the body. (To patient): Turn your head first to one side and then to the other. You see the movement of the head is quite free also. The symptoms in this patient seem to be referable chiefly to the spinal part of the meninges and if it were not for the positive Kernig's sign, present all through the illness, and if we ignored the findings in the cerebrospinal fluid, we might suppose we were dealing with a traumatic meningitis due to the lumbar puncture. But this is hardly possible. The Kernig's sign was positive before the lumbar puncture was made; in fact, lumbar puncture was suggested in the first instance by the presence of the Kernig sign. Moreover, the conditions under which the puncture was made, which are those employed in the routine of the hospital, were absolutely sterile. Finally, the degree of reaction is out of all proportion in the absence of infection, so I think we may safely rule out traumatic meningitis due to lumbar puncture.

Let us consider the single symptoms of meningitis now more or less in order. The head in the patient before us gives little indication of trouble. Headache has not been a prominent symptom. There is a little rigidity of the neck, but it is not marked, and there has been no retraction of the head. There is some little pain down the back and legs, but movement is not markedly restricted. Vomiting has been present all through the illness, and that is a definite, positive sign. The patient has had no vertigo, however, and there has been no psychic disturbance. Her temperature is quite high and has been so more continuously than is usual in purulent meningitis, where the temperature generally falls, after a time, to normal or nearly so, then rises again, and so continues an intermittent or a remittent course. There has been no strabismus, no anisocoria, and no pupillary disturbance—indeed, the movements of the eye

muscles are normal; in fact, there are no eye symptoms at all. Neither is there any facial twitching. The pulse has been irregular and rather slow, a sign that points strongly to meningitis. What has the pulse-rate been exactly?

STUDENT: At first it was frequent (105), and then it fell to 60, with some irregularity.

DR. BARKER: This behavior of the pulse points strongly to meningitis. On the other hand, Brudzinski's sign, as we have seen, is negative, though Kernig's sign has been present throughout. There is no evidence of either hemiplegic or aphasic symptoms. After this review of the single symptoms in addition to the laboratory findings, do you think we have to deal with a meningitis alone, or as an associated condition?

STUDENT: I should think it was meningitis from examination of the spinal fluid.

DR. BARKER: The spinal fluid certainly proves the existence of a meningitis, but you must remember that an acute encephalitis, a brain abscess, or a sinus thrombosis may extend to the meninges and be associated with a high temperature and with a high cell count in the cerebrospinal fluid. Nothing here points to sinus thrombosis, however; there is no dilatation of the cranial or facial veins, no swelling of the eyelids, no cyanosis of the orbital or frontal regions, no protrusion of the eyeballs, no engorgement of the retinal veins, no mastoid signs, no otitis media, nothing abnormal palpable in the jugulars.

I agree with you that we must make a diagnosis of acute purulent meningitis, but, supposing this to be correct, can we, returning to the etiology, definitely decide between a tuberculous meningitis and a non-tuberculous infection of the meninges?

STUDENT: The previous history of the patient and the family history of the patient are not suggestive of tuberculosis, though, in the colored race, tuberculosis is very common.

DR. BARKER: Well, the history, it is true, does not give important clues to etiology. Thus, for the non-tuberculous forms of meningitis, none of the antecedents commonly thought of has been present. There is no history of trauma, of otitis media, of disorder of the nose or of the paranasal sinuses, of infectious

diseases like typhoid or pneumonia; in short, of none of those conditions that may lead to pyogenic infection of the meninges by extension or by metastasis. On the other hand, there is nothing in the patient's heredity which we have elicited to make a tuberculous etiology probable except the general racial predisposition. Nor is there any evidence of a pre-existing tuberculosis of the bones or of the glands. How about the physical signs in the lungs?

STUDENT: There were some slight signs in the upper lobes, especially on the left side, both on physical examination and in the roentgenogram.

DR. BARKER: Yes; they were more than a little suggestive of a chronic pulmonary tuberculosis. Do you think that the long history of diarrhea could point to a tuberculous ulceration of the intestines? Was there any microscopic examination of the stools? Did anyone stain particles of mucus from the stools for tubercle bacilli?

STUDENT: Yes; a microscopic study of the feces revealed ova of *Trichuris trichiura*. We thought that the presence of this intestinal parasite probably accounted for the patient's long-standing diarrhea.

DR. BARKER: Your inference seems to me to be reasonable. Of course, whip-worm infection might also cause lesions that would serve as a portal of entry for germs that, passing through the blood, could lodge in the meninges. Still, the anamnesis clearly does not help us very much in this patient. The possibility of the existence of a chronic tuberculosis in the lungs, however, should not be lost sight of. Let us consider the manner in which the illness developed. Was the onset insidious, as it is in tuberculous meningitis, or was it a sudden, stormy onset like that so often seen in epidemic cerebrospinal meningitis?

STUDENT: It was, I think, rather insidious.

DR. BARKER: Well, though the onset was not stormy, it was rather acute. The patient was as well as usual up to January 20th, when she was taken ill. In speaking of the anamnesis, by the way, I have already referred to the question of race.

Both forms of meningitis occur in young colored people, but the tuberculous form is exceptionally common. Next, let us review again the findings in the fluid obtained by the lumbar punctures. The number of polymorphonuclear cells, as I told you, points rather to a non-tuberculous form of the meningitis. In tuberculous meningitis it is the lymphocytes in the cerebrospinal fluid that are, as a rule, the cause of the increased cell count. The bacteriologic examination of the fluid has not helped us up to the present time.

I notice a coagulum in this specimen of the spinal fluid that I have here. That coagulum should be carefully stained for tubercle bacilli. The fluid is not so very turbid now. What is the cell count for this specimen?

STUDENT: 900 cells. The count was made yesterday.

DR. BARKER: To sum up, then: since we have demonstrated the presence of neither the tubercle bacillus nor of any other organism in the fluid, we are unable as yet positively to decide the question of a tuberculous or a non-tuberculous origin of the meningitis in this case. One point, however, it is important just here to inquire into, and that is the possible presence in this vicinity of epidemic cerebrospinal meningitis at this time. I should like to ask Dr. Bloomfield if he knows of cases of that disease in Baltimore at present?

RESIDENT PHYSICIAN: There is one case here now in Ward I under Professor Janeway's care, and one in the pediatric service of the hospital under the care of Professor Howland.

DR. BARKER: This *may* mean the beginning of a meningococcic outbreak here. Moreover, sporadic cases are, as you know, sometimes met with, and when they enter hospitals, it is very desirable that a careful inquiry be made of conditions in the houses in which they lived, and, if possible, cultures should be made from contacts, especially from the nose and throat of the male parent. In this disease infection seems to be spread less by the patient himself than by healthy persons who come in contact with him. When children sicken of the disease it is often because the father has become a meningococcus carrier. The father becomes contaminated while at work, from some other

carrier, and then goes home and infects his child, presumably by kissing it, or by coughing. Sometimes the mother is the carrier, but not nearly so often as the father. In 1893 Dr. Flexner and I investigated an epidemic of cerebrospinal meningitis at Lonaconing and other mining towns in the valley of George's Creek, Maryland, where some 470 cases occurred in 350 families. The majority of these cases occurred in the families of miners. At that time we knew nothing of meningococcus carriers, and we were very much puzzled by the peculiar incidence of the disease, which was quite independent of the schools. The probability seems to be that one miner, who has become a carrier, infects a number of others in the mine in which he works, the moist, confined air of the mine and the close contact of the workers being favorable to the transmission of the germs from one workman to another. The contaminated miners, on going home, convey the infection to their children, though they remain healthy themselves.

The fact that there are cases of cerebrospinal meningitis in Baltimore at present increases the possibility that, in this instance, we may be dealing with a case of meningococcic infection, and after a little further study we may have some positive evidence to that effect.

There is one other possibility that we should consider before we conclude our discussion of the diagnosis in this case, namely, that the disease may be the meningeal form of poliomyelitis or, as it is better called, the Heine-Medin disease. In a certain proportion of cases of the Heine-Medin disease, commonly known as acute anterior poliomyelitis, and more commonly still as infantile paralysis, the virus localizes chiefly in the meninges, causing a real meningitis, though it is only part and parcel of the general meningomyelitic process that characterizes this dreadful infection. Netter believes that this meningeal variety is especially prevalent in France, and states that out of 58 cases of poliomyelitis that occurred in Paris during October, 1910, 17 were of the meningeal type, while in an outbreak of the disease that took place in the department of the Charonne in 1913, 9 out of 18 cases belonged to the meningeal variety. He

is convinced that up to recent years, before the development of more definite means of diagnosis, the condition was frequently mistaken for cerebrospinal meningitis, and that many epidemics of that disease (so-called) were really epidemics of poliomyelitis in which the meningitic type of the infection predominated. He cites as an example one outbreak which took place in 1901 at Loumis, in Switzerland, and was described by Walder as an epidemic of cerebrospinal meningitis, though paralysis was still present in a number of the cases after an interval of five years. He also points out that the two diseases (meningococcal meningitis and poliomyelitis) may appear in epidemic form at the same time and in the same countries, for, although they are essentially different diseases, with a wholly different etiology, the mode of propagation of the one seems to be very similar to that of the other disease.

An excellent account of the symptoms of the unusual forms of the Heine-Medin disease will be found in Wichmann's article, and also in the excellent monograph of Peabody, Draper, and Dochez. The symptoms of the meningeal form of poliomyelitis include vomiting, sometimes continued for forty-eight hours, followed by rigidity of the neck with flexion of the head. The patient may be soporous. The ankle-jerks are diminished. The Brudzinski sign and the Kernig sign are present, as is also Macewen's sign, though the latter may be only slightly marked. These symptoms and signs merely point to meningeal irritation in general, and may be due to cerebrospinal meningitis, to other forms of pyogenic leptomeningitis, to the tuberculous form of meningitis, to the meningeal form of poliomyelitis, or simply to a meningismus.

In all cases in which there is any doubt as to the diagnosis between meningitis and the meningeal forms of poliomyelitis we rely chiefly upon examination of the blood and of the cerebrospinal fluid. Dr. Josephine Neal, in a discussion of poliomyelitis before the New York Academy of Medicine last October, gave the following facts, obtained from her work in the New York Health Department, as guides to diagnosis based upon lumbar puncture. In the early stages of poliomyelitis the cerebro-

spinal fluid is clear except in a few rare instances, in which it is very slightly cloudy. It often shows a good fibrin-web formation. There is a slight or a moderate increase of albumin and globulin, together with a prompt reduction of Fehling's solution. The cell count is increased and, as a rule, 80 per cent. or even more of the cells are mononuclears, though occasionally, in those cases in which the fluid is slightly cloudy, the polymorphonuclears may predominate. In studying the cerebrospinal fluid Dr. Neal and other workers in the New York Health Department have frequently observed certain large mononuclear cells, which they believe to be, in a measure, characteristic of poliomyelitis. They are now investigating these cells by means of different stains, in the hope that their researches may develop something of definite diagnostic significance.

In the early stages of ordinary meningitis, on the contrary, the cerebrospinal fluid except in rare instances shows a varying degree of cloudiness. The increase in albumin and globulin is usually greater than that which occurs in poliomyelitis, and there is a poorer reduction of Fehling's solution. The cells in the spinal fluid of purulent meningitis are largely polymorphonuclears. The meningococcus can usually be found on careful search, though there are certain very mild cases, probably of the epidemic variety, in which the meningococcus may never be positively demonstrable in the fluid. When the meningitis is due to other organisms, they can practically always be found, sooner or later, either in smears or in cultures made from the fluid.

There remain, however, a few cases in which the differential diagnosis, even with the aid of the spinal fluid skilfully examined, is not devoid of difficulty. Netter attaches considerable importance, in these circumstances, to complete loss of the knee-jerk at a very early stage in poliomyelitis, and also to the presence of severe pain in the limbs, which he thinks is especially marked in the meningeal type of the disease. Neal says that in a certain small proportion of cases of this form of poliomyelitis the spinal fluid can only be differentiated from that of tuberculous meningitis by means of animal inoculations.

The possibility that we have to deal with the meningeal form of poliomyelitis in the case before us today is, in my opinion, remote. There is, as yet, of course, no bacteriologic evidence against it, but the turbid spinal fluid, the high cell count, and the large preponderance of polymorphonuclears point strongly toward meningococcal meningitis. Moreover, the patient has now been ill nearly three weeks, and if she were suffering from poliomyelitis in any form we should expect to see by this time some signs of paralysis, all the more, as the paralytic effects of the disease reach their acme early in its course. It should not be forgotten, however, that in the meningeal form of poliomyelitis the paralysis may be entirely limited to the ocular or facial domains. Koplik has seen a group of cases in which there was only unilateral ophthalmoplegia with hemorrhages into the retina.

One could, of course, inoculate a monkey with some of the cerebrospinal fluid and see whether or not the animal developed the Heine-Medin disease. But monkeys are rarely available for such differential diagnostic work. Moreover, in the present instance, the evidence in favor of a non-poliomyelitic meningitis is sufficiently preponderant to make the test seem unnecessary.

Treatment.—Before we close we must consider briefly the treatment of this patient. There is no doubt, in my mind, that we should treat this case as though it were one of meningococcic meningitis, and so give the patient the benefit of the doubt. The proper method to be employed in this treatment is, as you know, to remove some of the cerebrospinal fluid and then to inject some of the Flexner antimeningococcus serum. The amount of serum introduced should always be *less* than the amount withdrawn. This is undoubtedly the most effective treatment at our command. Even in tuberculous cases the mere removal of the fluid and the consequent decrease of pressure is often beneficial. Dr. Neal, in a recent report from the New York Health Department, lays stress upon the following points in carrying out the Flexner treatment:

"Two most common mistakes in serum treatment of epidemic cerebrospinal meningitis seem to be giving too few doses of the serum if the patient improves considerably after the first dose,

and failure to persist with the serum if the improvement is very slow."

The experience in New York is in accord with ours here. It is rarely safe to give less than four doses of serum on consecutive days even if improvement, clinically, is rapid and the organisms disappear from the cerebrospinal fluid. The usual number of injections required in cases of average severity is from three to seven. It is rarely wise to give a dose of more than 20 c.c. at one injection. It is the custom of the New York Health Department to give autogenous vaccines in all cases manifesting a tendency to become chronic. In a good many instances these vaccines have seemed beneficial, though the total number of cases in which they have been employed has, as yet, been too small, according to Dr. Neal, to demonstrate their real value. Captain Gaskell, R. A., has recently reported a case in the Home Army of Great Britain in which there was an extremely chronic condition of intermittent headache and other symptoms, which suddenly came to an end on the administration of 5 c.c. of the patient's own serum. In this case the autogenous serum was tried because experiments with it and with the serum supplied by the Rockefeller Institute for the use of the British Army showed the patient's own serum to be more agglutinative than the Flexner serum.

We had an outbreak of cerebrospinal meningitis in my service here at the Johns Hopkins Hospital in 1908. Our mortality at the hospital previous to the use of the Flexner serum had been about 75 per cent.; after we began to use the antimeningitic serum we had 70 per cent. of recoveries. Dr. Frank J. Sladen, who was at that time in charge of the infectious ward, made careful observations on the patients treated, and has reported them in a Fasciculus of the Johns Hopkins Hospital Reports. I advise you to look up his paper. Netter, in reporting the results obtained from the Flexner treatment in an outbreak of the disease in Paris in 1915, gives the gross mortality as 24.4 per cent., in contrast to 83.3 per cent. before its employment, and says that he believes the number of deaths would have been still smaller had it not been for the large proportion among

the patients of infants, who do not respond to the serum treatment as well as do older children and adults.

The increased number of recoveries from cerebrospinal meningitis since the introduction of the antimeningococcic serum has been so marked that when an epidemic of the disease made its appearance among the British soldiers in the Home Army, early in 1915, it was confidently expected that the mortality under serum treatment would be noticeably low. The actual results, however, have been the cause of much disappointment. Sir William Osler, in opening a discussion of the subject in October, 1915, at a meeting of the Royal Academy of Medicine, said that in one of the Canadian regiments stationed near Salisbury there had been 40 cases with 26 deaths, a mortality of 63 per cent., in spite of routine treatment with the Flexner serum. The cases were under the care of Dr. Ellis, who had been for several years at the Rockefeller Institute, and the sera employed were obtained from supposedly reliable sources, such as Burroughs, Wellcome & Co., the Lister Institute, Mulford, and Parke, Davis & Co. The same disappointing results in other parts of Great Britain and Ireland were reported by various persons taking part in the discussion, among them Surgeon-General Rolleston, who said that, from the beginning of the war up to July, 1915, 170 cases of epidemic cerebrospinal meningitis had occurred in the Royal Navy, with 89 deaths, in other words, with a mortality of 61 per cent. Sir William Osler said he believed that there was one main cause for this wide-spread failure, namely, *inert sera*, though insufficient dosage, failure to treat cases early, and imperfect technic were doubtless contributory. In the same discussion Dr. Gardner Robb, of Belfast, said that up to the time of the war he had had the same favorable results with antimeningococcic serum as others, the mortality in the hospital under his control during an epidemic in 1907 falling from 80 per cent. for the three months immediately preceding the introduction of the serum, to 26 per cent. for the four months immediately following it. Upon the reappearance of the disease he had confidently expected that they might look forward to even better results, and had been greatly disappointed to find that in exactly

100 cases which had come under his care the gross mortality was 36 per cent. He agreed with Sir William Osler that the present want of success was due to a difference in the quality of the serum, a difference which he believed to be explained by the fact that the great demand for it had been a strain upon the sources of supply in both Great Britain and America, the result of which was that all the available horses had been bled so frequently that the immunity value of the serum was seriously depreciated. For this reason, and possibly for others as well, he thought there was no doubt that much of the serum that reached England during the winter of 1914–15, was of a much lower standard than that of the serum formerly supplied. The preparation of serum, however, had been taken up again by the Rockefeller Institute and serum was now available that, judging by all laboratory tests, was of higher value than any formerly in use. He, himself, after some correspondence with Dr. Flexner, had visited the United States and brought back with him a supply of the new serum. Thus far he had used it in the treatment of 8 cases, with only one death, though one of the successful cases had been extremely unpromising.

These results have been confirmed by those obtained in the cerebrospinal laboratories throughout England. Surgeon-General Rolleston has recently reported that in 95 cases in the Royal Navy, treated with the new supply of serum during 1916, the mortality was 31.6 per cent., figures in marked contrast to those of the previous year, when the mortality in the Navy was 61 per cent.

Further Progress of the Case.—The patient made a slow but satisfactory recovery, though the diagnosis continued to be doubtful from an etiologic standpoint. On February 16th, three days after the clinic, at a fourth lumbar puncture, 20 c.c. of turbid fluid were removed. The cell count was 1081 and the Ross-Jones sign was positive. The polymorphonuclears still predominated, but there was a noticeable increase in the number of mononuclear cells. The Wassermann test was applied a second time to the fluid, with a second negative result. On the 25th of February a fifth lumbar puncture was made,

15 c.c. of colorless turbid fluid being withdrawn. The cell count was 600 per cubic millimeter. A smear made from the spinal fluid showed a majority of red cells; some fibrin; no bacteria; and numerous white blood-corpuscles, 90 per cent. of which were now mononuclears. Following the withdrawal of the spinal fluid, 20 c.c. of antimeningococcic serum were introduced by the gravimetric method. The injection was followed by severe headache, which had not been present after the lumbar punctures, but as soon as this passed off the patient began to improve. The rigidity of the neck became less and Kernig's sign, though still present, was much less marked. A sixth puncture was made on March 15th, 10 c.c. of slightly turbid fluid being removed. The cell count had diminished to 130 and practically all the cells were mononuclears. The Ross-Jones sign continued positive.

On March 21st the patient, whose condition was otherwise greatly improved, developed a partial deafness. She was somewhat drowsy, but, when roused, her mentality was clear. There was no headache, no rigidity, and the ear drums appeared to be perfectly normal. Three days later, March 24th, the deafness had passed off. On March 28th the pulse was normal and the temperature a little subnormal.

On April 4th the patient was up and about, and on April 10th the seventh and last lumbar puncture was made. The fluid withdrawn was still slightly turbid, but the pressure was reduced and the cell count was only 40 per cubic millimeter. The Ross-Jones sign, however, continued positive. On April 12th the patient felt perfectly well, with no headache and no lumbar pains or cervical rigidity. There was still a slight suggestion of Kernig's sign on the left side.

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CLINIC ON 2 CASES OF FIBRILLATION OF MUSCULAR TISSUE

January, 30, 1917.

We have today two interesting cases, in both of which the muscular system is out of order, but, whereas, in one of them the voluntary striped muscle of the skeletal system is involved, in the other it is the heart muscle which, although it also is striped, belongs to the involuntary system, that is affected. In both cases fibrillation is taking place in the muscular tissue, and it is interesting to observe the effects of fibrillation of these two different systems at the same clinic.

CASE I.—ATRIAL FIBRILLATION IN MITRAL STENOSIS AND MITRAL INSUFFICIENCY

The first case is one of *atrial fibrillation* or, as it is more commonly called by clinicians, *auricular fibrillation.* This condition affecting the atria (or the auricles) of the heart has been well understood only within the last five or six years. Though perpetual arhythmia was recognized by Mackenzie in 1890, when he was making a study of the irregularities of the pulse, it was not until some time after the application of the string-galvanometer to the study of disturbed cardiac mechanism that the true relation between fibrillation of the atria and the condition of perpetual arhythmia, known as the *pulsus irregularis perpetuus*, was clearly established. In 1909 Lewis, and also Rothberger and Winterberg, working independently, showed that electrocardiograms, taken from dogs after the atria had been set into fibrillation, were practically identical with those obtained from patients having an absolutely irregular pulse. At the present time atrial fibrillation is recognized as the cause of perpetual arhythmia, and the condition itself is established as a definite clinical entity. It is seen in many different affections of the heart and is of quite frequent occurrence, being

observable in over one-half of the cases admitted to the adult wards of a general hospital on account of heart failure.

The patient before us today is a young married woman, twenty-two years old, who does her own housework. She entered the hospital on January 12th, complaining of goiter and of palpitation of the heart. Her family history is unimportant except that her mother died of tuberculosis. She herself had the usual diseases of childhood, and also typhoid fever, followed by pneumonia, when she was eight years old. When she was ten or eleven she had an attack of rheumatism accompanied by fever, in which she was ill in bed, and another similar attack when she was seventeen. She says her joints were not affected in either of these illnesses. If her joints were not affected, how did she know the disease was rheumatism?

STUDENT: The doctor who attended her called it rheumatism.

DR. BARKER: Six months ago she had a slight attack of tonsillitis. She is subject to occasional headache. Her teeth are now well kept, but they show evidence of much suspicious looking dental work, and she says that they give her "a good deal of trouble." She has had no dyspnea before the present illness, but her heart has been beating very fast, she thinks, for a long time. This observation of hers is interesting in connection with the fact that she has been told that she has goiter. She says that she has never been especially nervous, though she admits that she is easily excited. Her appetite and digestion are good. She was married ten months ago. She has never been pregnant. There have been no symptoms referable to the genito-urinary tract. The Wassermann reaction is negative. Her weight last October was 144 pounds. As she weighed 163 pounds in August, 1916, she has evidently lost 19 pounds. What is her height?

STUDENT: I don't know exactly.

DR. BARKER: If you knew you could apply Dr. Guthrie's formula for the calculation of her ideal weight. We allow 110 pounds for a height of 5 feet and 5½ pounds for each additional inch. There are several other formulæ, for the determination

of the ideal weight of an adult, such as Von Noorden's, Bernhardt's, and Brocas, but you will find Guthrie's formula most convenient for quick orientation.

About two years ago the patient observed a swelling of the neck. A physician told her that her thyroid was enlarged, though she had no other symptom of thyreopathy except a tachycardia. Last August she went to a doctor for some medicine. At this point the history is a little contradictory, for the patient declares she still had no symptoms of any kind. Two or three weeks after taking this medicine she developed a pollikiuria. What is a pollikiuria?

STUDENT: Increase of frequency in urination without increase in the quantity of urine.

DR. BARKER: Two or three days after the appearance of this disturbance of urination, while the patient was sitting quietly reading, she noticed sudden palpitation of the heart, which has continued ever since. When was this exactly?

STUDENT: The first week in September, 1916.

DR. BARKER: Notice that the palpitation came on suddenly, while the patient was reading, and has continued ever since, keeping her awake a good deal of the night. When she got up the morning after this first attack of palpitation she fainted and was unconscious for from twenty minutes to half an hour. On recovering consciousness she had some nausea and vomiting, which continued for several days, and she was in bed altogether at that time for about two weeks. When she got up she felt weak and nervous. Early in November she had another attack of nausea and vomiting, lasting for about two weeks. I would have you notice the marked digestive disturbance complained of at that time; it is a question whether it was due to disturbance of the circulation, to overactivity of the thyroid, or simply to some primary digestive disorder. Since that time the patient asserts that she has been nervous and unable to read or to write on account of "spots in front of her eyes." She had a slight cough which she attributed to irritation in her throat; she has also been constipated, has suffered from headache, and has had, she thinks, a little jaundice. Her pulse, she was told by her

physician, varied in frequency from 120 to 180 beats per minute, and she has lost, as I have told you, 19 pounds in weight since August. In December she began to feel somewhat better. Since then she has been doing her own housework, which she had not been able to do before.

On admission to the Johns Hopkins Hospital (Professor Janeway's Service) the patient appeared to be a well-nourished woman, markedly dyspneic. She was distinctly flushed and was slightly cyanotic. Examination of the head was negative. The pupils reacted normally to light and to accommodation. Her tonsils were not enlarged; her pharynx was slightly injected. The thyroid showed some enlargement of the isthmus and of both lobes; it was soft, but there was no thrill, and no bruit could be heard over it. The epitrochlear glands were not enlarged nor was there lymph glandular enlargement elsewhere. The thorax is well formed and examination of the lungs was negative except for a few râles at the bases. Examination of the heart showed a marked pulsation at the apex, both visible and palpable. The heart was much enlarged, extending 16 cm. to the left in the sixth intercostal space and 4.5 cm. to the right, in the fourth intercostal space. A definite thrill was palpable over the apex-beat. The point of maximum impulse was in the sixth intercostal space, 14 cm. from the median line. The heart sounds were very irregular in force and rhythm, the first sound at the apex being rather snappy and followed by a marked systolic murmur. The heart's action was very rapid and there was marked cardiac arhythmia. A diastolic murmur was audible and I shall refer to it later. The radial pulse was small and irregular. A rate of 100 was counted at the wrist and a heart rate of 152 was counted at the apex—an outspoken tachycardia. The blood-pressure was $\frac{105}{70}$. Four conditions at once suggest themselves to account for the marked tachycardia:

(1) Paroxysmal tachycardia; (2) Graves' disease; (3) auricular flutter, and (4) atrial (or auricular) fibrillation.

When a tachycardia is associated with marked irregularity we can rule out flutter immediately. In the tachycardia of Graves' disease we have, as a rule, no arhythmia, and the

intervals between the ventricular beats are of equal length. When we have a rapid pulse with a profound irregularity of the intervals between the beats we are nearly always dealing with atrial fibrillation.

The abdomen, as you see, is normal in appearance. There was some tenderness over the liver and the liver dulness extended three fingers below the costal margin. To what is this tender liver due?

STUDENT: To stretching of Glisson's capsule owing to venous stasis.

DR. BARKER: Yes, I think that is the correct explanation of the tenderness. There was no pulsation over the liver. The spleen was not palpable. There was slight dulness in both flanks and slight edema in the ankles and over both tibiæ. The fingers showed no clubbing; there was slight sweating of the palms. The reflexes were normal. What did the blood examination show?

STUDENT: R. B. C., 5,012,000.
W. B. C., 11,720.
Hb., 75 per cent.
Differential count:
P. M. N., 65 per cent.
S. M., 17 per cent.
L. M., 13,5 per cent.
Transitional, 1 per cent.

DR. BARKER: How about the urine?

STUDENT: The output was small and it contained albumin, but no casts.

DR. BARKER: Now, why should this patient have an oliguria?

STUDENT: Because of the venous stasis in the kidneys.

DR. BARKER: Yes; there was a stasis nephropathy; the oliguria and the albuminuria were due to this. When the patient was admitted, she was kept at rest in bed on a cardiac diet for four days, and during that time 4 mg. of strophanthin were given without affecting her pulse-rate. She was then started upon a course of infusion of digitalis, after which the pulse-rate fell and there was marked diuresis, with a great change for the

better in the patient's subjective condition. In this first course of infusion of digitalis the patient received in all 24 fluidrams.

This failure of strophanthin to benefit the patient and subsequent immediate success of digitalis therapy makes me wonder whether the strophanthin used was what it should be. I have had two or three disappointing experiences recently in the use of strophanthin. Formerly we got excellent results with strophanthin in myocardial insufficiency, but recently I have found that the strophanthin used has sometimes failed, though we got excellent results with digitalis, as in this case. It may be one of the side results of the war that the strophanthin on the market is not so good as it should be. You should give strophanthin, by preference, intramuscularly; the pain and discomfort following an intramuscular injection are easily controlled, as a rule, with a hot-water bag. I do not advise intravenous injections of strophanthin unless there is great urgency; even then you should not give as much as a milligram at a dose. I have seen its administration intravenously followed by rigor and exitus. But, if it were absolutely necessary, I would give $\frac{1}{4}$ mg. of Bohringer's strophanthin by intravenous injection and repeat the dose in two or three hours, if it seemed indicated.

In this case, after the course of digitalis, the heart rate fell to 76 at the apex and the pulse-rate to 70 at the wrist. There was marked diuresis and the edema soon disappeared. Note by the chart how quickly the oliguria gave place to polyuria when the circulatory conditions improved and the renal stasis was reduced. The patient herself felt much better, and one day escaped from bed and walked about a little. After this exertion the pulse-rate rose and she was given another course of 12 fluidrams of infusion of digitalis, which again resulted in improvement of her condition.

Now let us compare the present condition of the patient with her previous state. The first thing we notice is that the size of the heart has changed markedly. The point of maximal impulse is now in the fifth intercostal space, 9.5 cm. from the median line. The area of cardiac dulness extends 11.5 cm. to the left. There is now a rather low-pitched diastolic murmur

audible at the apex and at the left border of the sternum. I would call your attention here to an interesting point, namely, the relation of this diastolic murmur to the second sound at the apex. When the atria are fibrillating the diastolic murmur usually has a fixed time relation to that sound. The murmur begins soon after the second sound, and if the heart rate is very rapid, it goes right up to the first sound of the succeeding beat, thus occupying practically the whole of diastole. When there is no more than a moderate tachycardia, the murmur maintains its relation to the second sound, but falls short of the first sound following it. With a slow pulse, say not more than 70, the diastolic murmur begins as usual after the second sound, but ceases so quickly that there is an interval of some length between the end of it and the succeeding first sound, the murmur being really confined to early diastole. Thomas Lewis lays it down that when mitral stenosis and atrial fibrillation "are present in the same patient, *and the heart rate is slow*, an early diastolic murmur, most clearly audible to the apex, but often spreading beyond it, is an expected sign." But this protodiastolic murmur accompanying atrial fibrillation with mitral stenosis is often a source of error, being supposed by medical students and sometimes by physicians to be a murmur due to aortic insufficiency. This is a common mistake, but a diagnosis of aortic insufficiency, when the heart is slow as well as very irregular, is never justifiable unless unequivocal signs of aortic insufficiency apart from such a murmur are present. Never forget that uncomplicated aortic insufficiency very rarely coexists with atrial fibrillation, whereas mitral stenosis and atrial fibrillation, as Lewis says, are "bosom companions." "The early diastolic murmur of mitral stenosis is relatively soft in quality and it usually begins a little later than the second sound. The absence of a water-hammer pulse and of a murmur at the aortic cartilage are evident aids to a correct conclusion."

The predominating features in the case before us are: (1) the perpetual arhythmia; (2) the loud, blowing, systolic murmur following the first sound, and (3) the short protodiastolic murmur. The electrocardiogram shows an absence of the normal pulse

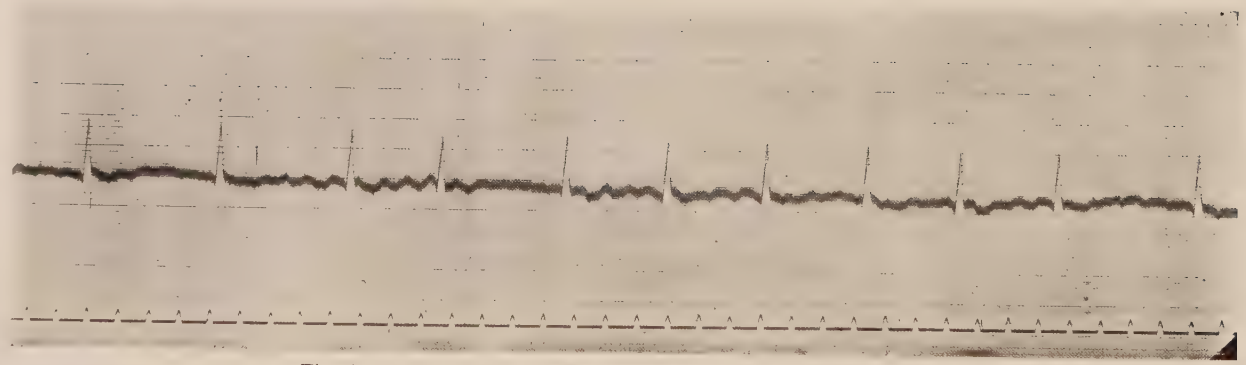

Fig. 6.—Electrocardiogram, Derivation I, showing atrial fibrillation.

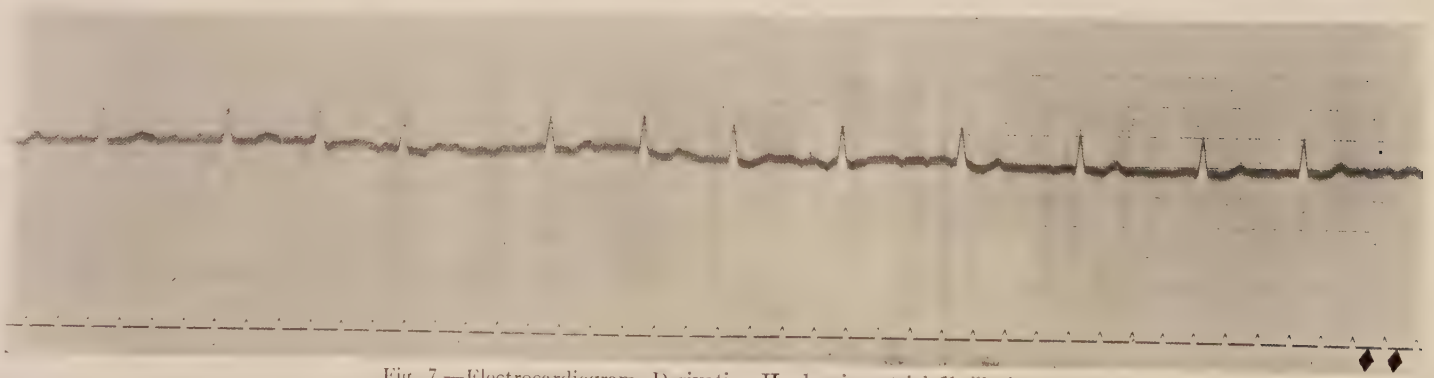

Fig. 7.—Electrocardiogram, Derivation II, showing atrial fibrillation.

waves, irregular ventricular sequence, and coarse fibrillation waves between the ventricular complexes. (*Electrocardiogram passed round for examination*). This, of course, justifies a diag-

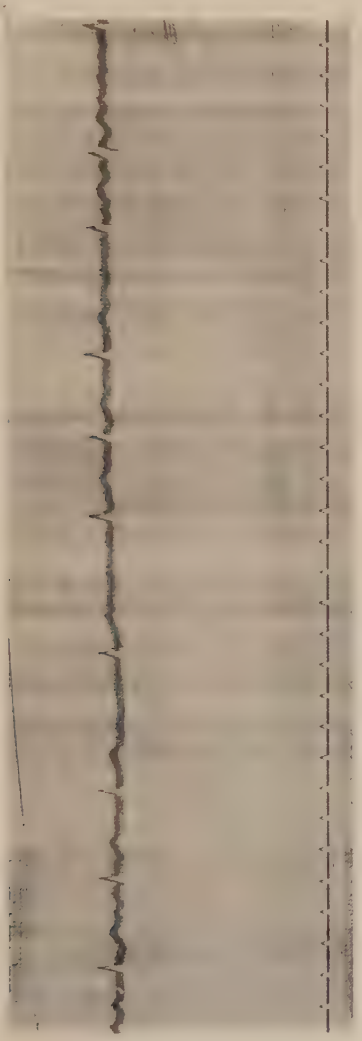

Fig. 8.—Electrocardiogram, Derivation III, showing atrial fibillation.

nosis of atrial paralysis and atrial fibrillation. After you have studied a case of this kind with the aid of the electrocardiogram, it is easy, in most cases, to make the diagnosis simply by feeling

the pulse and listening to the heart. The irregular intervals between the systoles is so characteristic that one could scarcely be deceived, even when employing simply auscultation and palpation of the heart-beat and the radial pulse. Remember that a heart rate between 120 and 150, with markedly irregular action, is almost always due to atrial fibrillation. A slow heart with irregular action may sometimes be met with in atrial fibrillation, but it may also be due to the presence of extrasystoles or to a partial heart-block. You can often decide whether you have to do with atrial fibrillation or with an extrasystolic irregularity in such a case by making the patient sit up and then lie down again two or three times in succession. If you have to do with an irregularity due to extrasystoles, the exertion, accelerating the heart, will cause the pulse to become more regular; if, on the other hand, the irregularity is due to atrial fibrillation, it is only increased by the exertion and the acceleration. Another point to remember is that if you have a marked tachycardia with irregularity and the irregularity becomes more prominent on slowing of the heart rate, you are probably dealing with an extrasystolic irregularity. There are fewer premature contractions when the heart rate is rapid than when it is slow. In atrial fibrillation, on the contrary, the irregularity does not disappear even when the heart slows; there is a perpetual arhythmia. If you are in doubt as to the existence of arhythmia, take a little strip of an arteriogram, or of an apex cardiogram, and measure the intervals between succeeding systolic waves. In arhythmia you will find that hardly any two beats are equally distant.

In the condition known as *atrial flutter* you have a regular ventricle, but the impulses, instead of arising in the normal place, originate in abnormal sites in the atria as a result of pathologic automatic impulses. The rate of the atrial contractions thus arising and transmitted through the conduction system is so great that the ventricles can rarely keep the pace. The usual rate of the atria in this condition of "flutter" is 260 to 320 a minute, while the ventricular rate at the same time will be only from 130 to 175. The conduction system is unable to transmit more than one-half, one-third, or one-quarter of the

impulses. In other words, you have a two-to-one heart-block, or in some cases a three-to-one or even a four-to-one block. In atrial flutter it is believed that the pathologic stimuli arise at a single focus in the atrial tissue situated at some distance from the normal "pacemaker" and ungoverned by the cardio-inhibitory nerves. As Lewis expresses it:

"The reins of control, the inhibitory nerves, are powerless and the auricle (atrium) has veritably seized the bit between its teeth, while the ventricle, shielded from the whip by the auriculoventricular bundle, lags behind."

Sometimes you have a complete dissociation of the ventricular from the atrial activities, in which case the atria may be beating 300 times per minute, and the ventricles only 30 to 40 times in the same space of time. But in the ordinary flutter of older people (between fifty and sixty years of age), commonly due to arteriosclerosis, an atrial rate of 300 is generally accompanied by a ventricular rate of one-half, one-third, or one-fourth.

Let us now, after this slight digression, return to the question of the nature of *atrial fibrillation*, the condition existing in the patient before us, and compare it with the condition just referred to as atrial flutter. If the heart of an animal in the condition of atrial fibrillation be closely observed, it will be seen that the muscle surface of the atrium is maintained in a position of diastole and is in extreme and incessant activity, rapid and minute twitching and undulatory movements being visible all over it without any effective contraction of the wall of the atrium as a whole. The nature of the fibrillation is still somewhat obscure. The theory that has received most consideration is that of Lewis, who considers that the fibers of the auricles no longer contract co-ordinately or together, and the impulses that normally succeed one another at regular intervals no longer are sent to the ventricles. Instead, a great many rapid and haphazard impulses, arising in a number of small, independently active areas in the atrial walls bombard the conduction system, though only a small proportion of them actually get through the bundle of His to the ventricles. Those that do, produce contractions

of the ventricle that follow one another at completely irregular intervals, and induce a state of perpetual arhythmia, so-called because, when the atria once begin to fibrillate, the condition, as a rule, is permanent. In atrial flutter, on the other hand, restoration of a regular rhythm is not uncommon, though, strange to say, when flutter changes to normal rhythm a temporary arhythmia due to a fibrillation of short duration may mark the transition. Paroxysmal fibrillation does occur occasionally, and when it does it is apt to be confused with simple paroxysmal tachycardia.

The essential cause of atrial fibrillation, although it is of considerable clinical importance, still remains obscure. Two general possibilities are admitted in regard to it: first, that there is some pathologic change in the muscle-fiber of the atria which renders them so prone to fibrillate that some sudden strain or the cumulative effect of prolonged overwork, such as might occur in valvular disease, is sufficient to initiate the process. The second possibility is that some extrinsic stimulus, such as an alteration of the blood-supply to the atria or a change in the chemical composition of the blood itself, would if sufficiently marked, cause fibrillation in a previously healthy heart, and still more readily in one already diseased. Canby Robinson points out that clinical experience is in favor of the first possibility because atrial fibrillation usually occurs in patients with cardiac lesions that are clinically demonstrable, especially with such lesions as throw an extra strain upon the atrium. Nevertheless, cases have been observed in which fibrillation took place in apparently healthy hearts, and in this connection he cites a case of his own that seems to afford evidence that atrial fibrillation may be set up in a healthy man by means of a wholly extracardiac factor. This case is of such interest that I would like you to know a little about it.

The patient was suddenly overcome with the fumes of hydrogen sulphid while at work in a chemical factory in St. Louis, and was taken to the Barnes Hospital. On admission it was noted that his pulse was irregular and the electrocardiograms showed that the irregularity was the result of atrial fibrillation.

The man did not seem seriously ill, and he recovered from the effects of the poison within a few hours. His pulse became regular again and the electrocardiogram showed that the heart had resumed its normal mechanism, the atria beating regularly, while pulse-waves of normal appearance occurred before each ventricular complex and the numerous small irregular waves due to atrial fibrillation entirely disappeared. The heart was not enlarged and percussion showed the cardiac dulness to extend 3.5 cm. to the right and 10 cm. to the left of the median line. The heart sounds were clear and of good quality throughout and the blood-pressure was $\frac{120}{75}$. The Wassermann reaction was negative and the patient had never had a serious illness of any kind in his life. He left the hospital in three days, apparently a healthy, normal man, and resumed his work in the factory. Some little time afterward he was reported as well in every way.

In this case the hydrogen sulphid was apparently the cause of the atrial fibrillation, but it is impossible to say whether it acted directly, either upon the atrial musculature or the nervous centers controlling cardiac activity, or indirectly, through changes in the blood. Its action, apparently, produced no permanent damage.

Now before we pass on to the second case before us this morning I should like to say a word as to the therapy to be employed in this class of disorders. The object of all treatment in a case such as this is, of course, to slow the rate of the heart and to maintain the power of the cardiac muscle. You have to do here with a condition of mitral stenosis in which the blood must pass through a narrowed mitral orifice, and associated with this you have a heart rate of 160 beats to the minute. Remember that in atrial fibrillation combined with mitral stenosis the atrium is not contracted, that the intervals between ventricular systoles are very short, and that there is only a little bit of a hole between the left atrium and the left ventricle for the blood to pass through, and you will be able to form some idea of how small an amount of blood can actually trickle from the atrium into the ventricle in each diastolic period, and you will

realize that an engorgement of the pulmonary circulation must result.

The remedies of most service in such a state of the heart's action are *digitalis* and *strophanthus*, both of which cause a delay of conduction in the bundle of His, thus impeding the passage of impulses from the atrium and reducing the number of stray impulses that can get through to the ventricle. If we can keep the ventricular rate down to 70 there is time, even in atrial paralysis and in severe mitral stenosis, for a good deal of blood to trickle through into the ventricle during each diastole. The mere reduction of the ventricular rate causes a wonderful restoration of the whole circulatory condition. In this class of cases the effects of the administration of digitalis may be truly marvellous; the therapy of no other cardiac disorder is as satisfactory as that of a well-managed case of atrial fibrillation. Digitalis is here life saving and life giving. Patients like the one we have here today can be "kept going" for years, even though the atrium does fibrillate, if the heart rate be kept down. At the beginning of treatment, when there is marked cardiac delirium, a bandage around the abdomen, causing compression, is often of great service, especially during acute attacks of palpitation. But our chief reliance must be upon rest and digitalis. As to the amount of the drug required, enough should be given to slow the heart, but not enough to evoke toxic effects. To get successful results with digitalis therapy some experience is necessary. One has to learn just how much to give, what preparation to use, and how best to use it so as to get the most beneficial effect without causing digitalis intoxication, which is shown by loss of appetite, nausea, and vomiting. Occasionally it may be necessary to push the drug administration actually up to slight intoxication in order to obtain the fall of heart rate desired. A heart rate of above 100 in atrial fibrillation when the patient is at rest is an indication for some preparation of digitalis or strophanthus in amounts sufficient to reduce the heart rate to 80 or lower. The tincture or the fresh infusion is the best form in which to administer digitalis. For adults, doses of 10 to 15 minims three or four times a day, if the tincture be

employed, or of 1 to 1½ fluidrams three times a day, if the infusion be used, will, as a rule, suffice. Usually the full reaction is obtained when 6 to 8 fluidrams of the tincture, or an equivalent amount of the infusion, have been administered. When the heart rate has been reduced to 80 the drug may be discontinued, but when the patient gets out of bed it may be necessary to resume it in small doses, say 5 minims of the tincture three times daily.

As a further guide to the administration of digitalis Canby Robinson recommends ascertaining the number of heart-beats per minute that fail to produce an arterial pulse-wave. To determine this the ventricular contractions are counted for at least one or, better still, for two minutes by means of a stethoscope over the precordium, after which the radial pulse is counted for the same length of time. The difference between the ventricular rate and that of the radial pulse is what we are accustomed to call here, after George Draper of New York, "the pulse deficit." As the heart's efficiency improves under digitalis therapy there is a marked lessening of the pulse deficit.

After the ventricles have slowed to about the normal rate it is necessary to find the dose of digitalis that, given over a long period of time, suffices to maintain the normal ventricular rate without causing toxic symptoms. To ascertain this Canby Robinson's procedure seems to be a very good one. He first reduces the dose to 2 or 3 minims of the tincture three times daily, and then gradually increases this until the heart attains what appears to be its best efficiency. I am of his opinion, that all cases of permanent atrial fibrillation should be kept under the influence of digitalis either constantly or intermittently, and my colleagues here, Professor Thayer and Professor Janeway, who see many cardiac cases, feel the same way.

Under this treatment, with careful attention to diet, to fluid intake, to habits of life, and to the avoidance of excessive physical exertion, patients with atrial fibrillation often live in comfort for a long time. Pardee, writing on the prognosis of this affection, has recently reported 7 cases of patients who under his observation for periods varying from seven months to three years had

been able to carry on active lives almost without restriction. The prognosis of atrial fibrillation has been generally believed to be worse than it really is, though Pardee emphasizes the fact that with hospital patients it is extremely important to keep them under observation for some little time after they have left the hospital, since the increasing exertion that they make on returning to ordinary life frequently necessitates the resumption of a digitalis therapy that had been discontinued, or the increase of a dose that had been sufficient to control the heart rate while the patient was under hospital conditions.

Before I conclude what I have to say concerning this patient I will call your attention to the fact that I have employed the term *atrial* fibrillation instead of *auricular* fibrillation, with which you are probably more familiar, throughout the discussion. I have done so, first, because I believe *atrial* to be the more correct term, and, second, because it is sure to be in common use in the future. *Auricle* may be the accepted expression for the moment, but *atrium* is a much better one, and I would strongly advise you to accustom yourselves to the use of it. It may sound strange to unaccustomed ears, but it is the B. N. A. term and is now generally accepted by anatomists. The term *auricle* is now reserved for the structure formerly designated *auricular appendix*. The coming generation of medical students will be familiar with the B. N. A. nomenclature from the beginning and will employ atrium as a matter of course, but those already in the profession will naturally have a little difficulty in becoming accustomed to the change from the old terminology to the new.

Further Progress of the Case.—The rate of the patient's heart varied markedly according to her posture; the average rate while lying down being 60 to 70; while sitting up in a chair, 86 to 100. The rate was much increased by slight exertion. About a week after the clinic the digitalis was discontinued on account of nausea and headache, which disappeared when the administration of the drug was stopped. After a few days the use of digitalis was resumed. At the end of about six weeks from the time of entering the hospital the patient's condition

was much improved. She had no cough, no dyspnea, and no edema, though the pulse remained absolutely irregular. She was discharged from the hospital as "improved" on February 26, 1917.

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CASE II.—PROGRESSIVE (CENTRAL) MUSCULAR ATROPHY (VULPIAN-BERNHARDT SUBVARIETY OF THE ARAN-DUCHENNE TYPE)

The second case before us today is one of progressive (central) muscular atrophy, a disease in which one of the characteristic symptoms is fibrillation of the voluntary skeletal muscles. In this affection different groups of muscles undergo gradual atrophy until, in extreme cases, the patient becomes literally skin and bone. The so-called "living skeletons," who make a livelihood by exhibiting themselves in cheap museums, are usually examples of this disease in its most intensified form. E. W. Taylor, in 1900, examined sections from the spinal cord of a man who supported himself until his death in this manner, and reported the findings, though he gave no clinical description of the case. Progressive muscular atrophy was first described by Van Swieten in 1724. In 1854 an Englishman, William Roberts, published a monograph entitled *An Essay on Wasting Palsy*, which contains an excellent account of the progress of knowledge concerning the disease up to that date. In 1849 Duchenne had presented a memoir on *Atrophie musculaire avec transformation graisseuse* to the *Institut de France*, and in the following year F. A. Aran had published a paper with the title

Recherches sur une maladie non encore décrite du système musculaire in the *Archives générales de médicine.* Ever since then the names of Aran and Duchenne have been intimately associated with this affection, though the condition as described by them is now considered to be only one special type of a disease that manifests itself in several different forms.

The patient before us this morning, John M., a man forty-six years old, complained, on admission to the hospital on January 23d, of twitching in the arms and legs, together with loss of strength in them. His family history is negative. I would have you notice this point, as the absence of familial and hereditary tendency is important in the differential diagnosis of a case of this kind. In one form of muscular atrophy, wholly different from the type before us, inheritance is a marked characteristic; my predecessor in the chair of medicine here has reported an instance of one family in which 13 members were affected in the course of two generations. The form we study today is neither hereditary nor familial. This patient, though a Swede, has lived in this country twenty-six years. He has always been well except that he has heavy colds every winter. With these colds he has a cough, but he says that it has not been "chronic." He also has suffered from headaches and has, all his life, been subject to faintness after working in the sun on hot days. He has been married twenty-three years and has 7 children, living and well. His wife has had two miscarriages, due, he says, to "accidents"; one child was still-born at term. The patient, a woodsman, accustomed to work for ten hours a day rolling logs, has been much exposed to wet and to extremes of heat and cold. This point may be of some importance, because hard work and exposure to the elements, in addition to *potatorium*, are the chief injurious influences that we have been able to elicit in the anamnesis of this patient. By the way, you will find the term *potatorium* a useful one. Do you know what it means?

STUDENT: No.

DR. BARKER: It is a euphemistic term for alcoholism, and therefore useful when you wish to avoid a blunt reference to

the subject that would be embarrassing in a patient's hearing. What information have you in regard to the potatory habits of this man?

STUDENT: The patient says he usually takes about 1 pint of whisky a day for three days at a time and then stops altogether for about two months.

DR. BARKER: Yes; he asserts that he is a teetotaler between whiles. He does not seem to be quite what we used to call in Canada a "quarterly drunkard." Some drinkers of this description are total abstainers for about three months at a time and then get drunk again. Quarterly drinking is one type of dipsomania.

The patient's present illness began, he says, in April, 1916, when he noticed twitching in the muscles of his right upper arm. Observe the site at which these twitchings began, because it is unusual to have this disease begin in this particular area. He says he could not only feel the fibrillations, but he could see them. About one month later he began to lose strength in his right arm. Here again is a point to be emphasized, namely, that he first noticed twitching and one month later became conscious of loss of strength; in other words, the fibrillation was followed by paresis. The twitching extended later to the muscles lower down in the right arm and in the right hand, and about the time this extension took place he also perceived twitching in his left arm. In short, his condition became progressively worse. Here is still another point to be noted—the trouble, after beginning in the right arm, extended to the left arm, there being an interval between its appearance on the right and left sides. This is what we should expect, for this disease, usually unilateral at first, often begins in the muscles that are most used. Eulenberg has given a number of instances in which overuse of certain muscles preceded the appearance of atrophy, and Schneevogt cites the case of a sailor in whom it developed in the right deltoid after he had been obliged to pump for days together on a leaking ship. Loss of function in the muscles is coincident with the wasting. As Roberts says in his interesting early description of the disorder:

"The tailor discovers that he cannot hold his needle; the shoemaker wonders that he cannot thrust his awl; the mason finds his hammer, formerly a plaything in his hand, now too heavy for his utmost strength; the gentleman feels an awkwardness in handling a pen, in pulling out his handkerchief, or in putting on his hat. One man discovers his ailment in thrusting on a horse's collar; another, a sportsman, in bringing the fowling piece to his shoulder."

Ultimately the disease almost always becomes bilateral. In this patient it grew gradually worse in both arms and extended, as I have said, down to the hands.

This man has had no pain in the muscles, though there was some slight pain of an aching character in his joints. At times he experienced, he says, a feeling of faintness. The question of pain in this connection is interesting. I have seen patients with this disease who had pain in the muscles at onset. You notice, there was in the man before us no subjective disturbance of sensation except the slight pain in the joints, and this raises the question whether this was due to a trophic arthropathy or to a true infectious arthritis. The probabilities are in favor of a trophic arthropathy because experience has shown that this is a common accompaniment of this disease. The patient also tells us that he has felt dizzy at times and more sleepy than formerly. Though he noticed that his arms became easily tired, he has not been conscious of trouble in any other part of his body.

Examination on admission showed that the man was poorly nourished. There was no dyspnea, no cyanosis, and no orthopnea. His mentality and orientation were normal. Marked fibrillary twitching could be seen plainly in both shoulders and both arms. The tongue, which could be steadily protruded in the median line, and which did not deviate to the right or to the left, showed distinct fibrillations in its substance. The epitrochlear glands were palpable. The thorax showed effects of emaciation and there was constant visible twitching of the thoracic muscles. Examination of the heart and lungs was

negative. The whole interest of the case centers, in short, in the locomotor system.

On inspection of the patient you can all of you, even those at a distance, I think, see something that is of interest, namely, the fascicular twitching of the muscles of the left shoulder and of the upper arm, involving also the pectoral muscles of the chest and the muscles of the right shoulder. You perceive it also, though less markedly, in the biceps of the right arm and in the muscles of both forearms. You can see almost a "dancing movement" of the muscles in the forearms on both sides. This is sometimes so pronounced as to be called "muscular madness" (*folie musculaire*). There is some slight twitching in the little muscles of the hand. Sometimes you have to stir it up by striking the hand, but usually exposure to cold will set it in action. You are struck at once by the fact that the fibrillation in the extremities is more marked proximally than it is distally; in fact, in the proximal regions the twitching is very extensive indeed. This fibrillation, though very characteristic of the disease, is not invariably present. Dr. H. M. Thomas has reported an instance where the disease occurred in a brother and sister: the fibrillary twitching was marked in one case and altogether absent in the other. There has been very little shrinkage in the thenar and hypothenar eminences, though they look a little wasted. The thenar eminence of the right hand is flatter than that of the left one. The interossei muscles show fibrillation and there has been some little interosseous atrophy. On looking at the palms you see that there are depressions between the metacarpal bones in both hands due to the wasting of the lumbrical and interossei muscles. In this disease the hands are often affected quite early, the usual explanation being that already mentioned—that the muscles most in use are those most likely to show alteration soonest, because they become more or less exhausted. (To patient): Have you noticed any difficulty in using your hands?

PATIENT: It is hard to use them.

DR. BARKER: What do you find it hard to do with them?

PATIENT: To use the fingers.

DR. BARKER: Please take hold of my finger between your thumb and forefinger. You see he has difficulty in doing so. (To patient): Do you also find it difficult to raise your arms?

PATIENT: Yes.

DR. BARKER: Grip my hand. You see there is very little grip in his hand. It is much less than normal. (To patient): Will you lean forward a little. In this position you can see twitching in the muscles of the back. The trapezius, the rhomboideus, the serratus, in fact, all the muscles that are visible, including the triceps in the back of the arm, can be seen to fibrillate. I do not notice any twitching in the muscles of the face. Now let us examine the lower extremities. (To patient): Have you noticed any twitching in your legs?

PATIENT: No.

DR. BARKER: When fibrillation appears in the legs it usually does so first in the flexor muscles, but I see none, at the moment, in the thighs nor any in the muscles of the calves. Did anyone in the ward observe twitching in the lower extremities?

STUDENT: A little.

DR. BARKER: The lower extremities are evidently nearly free from fibrillation thus far. In this case fibrillation began in the proximal muscles of the upper arms and extended down to the hands. On examining his hands, though you notice the definite wasting of the muscles, he has not yet got the hand peculiar to the first stage of the disease when it follows its commonest course. When the thenar eminence and the muscles around the thumb are atrophied, the first effect is to flatten the eminence and to interfere with the abduction and opposition of the thumb, so that the hand resembles that of a monkey—the *simian hand* (*main de singe* of Duchenne). The thumb is drawn backward by the long extensor muscle, so as to be in a plane with the other metacarpal bones, and the metacarpal bone is rotated somewhat on its own axis. This "simian hand" results from atrophy of the M. abductor pollicis brevis, the M. flexor pollicis brevis, and the M. opponens pollicis—all innervated, you will recall, by the N. medianus. Sometimes the atrophic process affects chiefly the muscles innervated by the N. ulnaris, leaving

those supplied by the N. medianus intact for a while; the Mm. interossei and Mm. lumbricales then become involved, first recognizable by inability to bring the fingers together when they are spread apart. Flexion of the proximal phalanges upon the metacarpal bones becomes impaired, as well as extension of the second and third phalanges, until, eventually, owing to the action of the muscles that are antagonists of the interossei, the first phalanges remain overextended, while the second and third are flexed so as to curve toward the palm, producing the second type of hand met with in the disease, known as the *claw hand* (*main en griffe*). Finally, all the hand muscles may become involved in the atrophic process, and the hand itself hangs loosely, with the fingers in extension, constituting the third type, called the *skeleton hand* (*main de squelette*). This third type—a combination of the simian hand with the claw hand—is often spoken of as the hand of the Duchenne-Aran type of muscular atrophy. In typical cases of progressive muscular atrophy, therefore, the hand may show any one of three main varieties of distortion occasioned by the atrophy of specific groups of muscles, varieties that are known respectively as the *simian*, the *claw*, and the *skeleton* hand. You should not forget, however, that these distortions of the hand may occur in maladies other than progressive (central) muscular atrophy. Since the paper of Mme. Déjerine-Klumpke in 1889 we look upon such distortions of the hand merely as syndromes that may have any one of several different causes (myelopathic, neuritic, or myopathic). Have any electric tests of the muscles of this patient been made yet?

STUDENT: Not yet.

DR. BARKER: As a rule, the muscles pass through all stages, from that of partial reaction of degeneration to the complete reaction of degenerative atrophy. At first there is a gradually developing atrophy demonstrable by the faradic and galvanic currents. Later the faradic irritability may be lost and the galvanic formula may be reversed; later still all the electric irritability of the affected muscles may disappear. It will be very interesting to ascertain whether these muscles show any changes in electric reaction.

Under what form of atrophy does this case most probably belong?

STUDENT: The progressive central form.

DR. BARKER: Yes; it is almost certainly non-peripheral. The characteristic pathologic changes are atrophy and degeneration of the nerve cells of the anterior horns of the spinal cord. The motor nerves, undergoing secondary atrophy, contain fewer fibers than normal. Let us now test the reflexes. You see the arm-jerk is overactive and the knee-jerk is very active. No patella-clonus and no ankle-clonus can be elicited on either side. The Babinski test is negative on both sides. The exaggerated reflexes in the arms and knees suggest that there may be not only atrophy of the anterior horns, but a beginning degeneration of the pyramidal tracts as well, in which case we should have to think of an amyotrophic lateral sclerosis. But if the pyramidal tract is touched, it can be only very slightly involved, for it has not undergone change enough to give rise to a positive Babinski reaction. Later on, perhaps, we may find some further evidence of degeneration of the pyramidal tracts. As Dr. H. M. Thomas has always emphasized, there is every gradation between amyotrophic lateral sclerosis and the pure anterior-horn or nuclear type of atrophy.

If we wish to subdivide the chronic progressive (central) muscular atrophies into groups, we may use Marburg's classification as follows:

A. Amyotrophia nuclearis progressiva.

(*a*) Spinal forms.

1. Aran-Duchenne type.

(Subvariety: Vulpian-Bernhardt type.)

2. Werdnig-Hoffmann type.

(*b*) Bulbopontile forms.

(Chronic progressive bulbar paralysis of Duchenne.)

(*c*) Pontomesencephalic forms.

(Chronic progressive ophthalmoplegia.)

B. Amyotrophic lateral sclerosis.

In setting up these types, however, we must keep ever in

mind the fact that they run over into one another, many transitional forms being met with.

In the *spinal forms of progressive (central) muscular atrophy* the muscles that undergo atrophy are those that are innervated by the lower motor neurons the cell bodies of which are situated in the anterior horns of the spinal cord. Under the spinal forms are included: (1) the Aran-Duchenne type, in which the atrophy begins in the thenar group of muscles of the hands, gradually involves the other muscles of the hands, and then spreads proximalward to the other muscles of the upper extremities; (2), the Werdnig-Hoffmann type, also known as the infantile, familial, and hereditary form of progressive (central) muscular atrophy, in which the atrophy begins in the muscles of the pelvic girdle and of the trunk, later involves those of the shoulder-girdle and neck, and finally extends to the muscles of the upper and lower extremities beginning proximalward and gradually passing distalward to the muscles of the hands and feet. In this Werdnig-Hoffmann type fibrillary twitching is absent, though scoliosis, club-foot, and flexion contractures are common accompaniments.

In the *bulbopontine forms of progressive (central) muscular atrophy* [paralysie musculaire progressive de la langue, du voile, du palais, et des lèvres of Duchenne] the muscles that undergo atrophy are those that are innervated by the lower motor neurons the cell-bodies of which are situated in the motor nuclei of origin of the cerebral nerves in the medulla oblongata and the pons. The nucleus N. hypoglossi (N. XII), the nucleus ambiguus (N. X), and the motor part of the nucleus N. trigemini (N. V) are commonly involved. Occasionally a part of the nucleus N. facialis (N. VII) also degenerates. The first symptom is usually a subjectively experienced difficulty in articulation. The pronunciation of R, of Ch, and of I may first be interfered with; later on the letters S, L, K, G, and T are found hard to pronounce. After atrophy of the lips sets in, the pronunciation of the labials, P, F, B, M, and W, may become impossible. Along with the disturbance of speech there develops difficulty of swallowing and also, sometimes, difficulty in chewing. These

three symptoms—dysarthria, dysphagia, and dysmasesia—are cardinal symptoms of the disorder, though please remember that the same three symptoms may occur in certain other diseases, for example, in pseudobulbar paralysis and in myasthenia gravis. You should not forget that attacks of dyspnea or of tachycardia in association with speech disturbance may point to a degeneration of the motor nucleus of the N. vagus.

In the *pontomesencephalic forms of progressive (central) muscular atrophy* the muscles that undergo atrophy are those that are innervated by the lower motor neurons the cell-bodies of which are situated in the motor nuclei of the eye-muscle nerves. As you know, the nucleus N. oculomotorii (N. III) and the nucleus N. trochlearis (N. IV) lie in the midbrain or mesencephalon, whereas the nucleus N. abducentis (N. VI) lies in the pons. When, in this disease, the chronic degenerative atrophy affects predominantly the eye muscles (chronic progressive ophthalmoplegia) we speak, therefore, of a "pontomesencephalic form" of the malady. It is rare that the atrophy and paralysis are limited to the eye muscles; as a rule, the ophthalmoplegia is associated with bulbar or spinal paralysis.

In *amyotrophic lateral sclerosis* we have a condition in which spastic phenomena (exaggerated reflexes, clonus, rigidity) due to degenerations of the pyramidal tracts are associated with one or another of the above forms of muscular atrophy due to nuclear degeneration. In the classical type, described by Charcot, the clinical picture begins as the Aran-Duchenne type of spinal nuclear atrophy; later spastic phenomena appear, and finally bulbar paralysis sets in. In the Kahler-Strümpell type the spastic phenomena appear first and the muscular atrophy reveals itself only later; or, sometimes, the reverse is true, the atrophy being pronounced from the beginning, slight spastic phenomena appearing later on. Still other combinations of spasm and of nuclear atrophy have been met with, but it would only be confusing, in the present state of your knowledge of this disease, to go into these in detail.

In the patient before us we know that the lesion must be central, rather than primary in the nerves or in the muscles,

because of the fibrillation; in primary myopathies (Landouzy-Déjerine type, Erb's type) there is no fibrillary twitching. We deal here with a nuclear disease of the spinal cord—a chronic myelopathy. If you will keep in mind certain diagnostic criteria, namely, the steadily progressive character of the atrophy accompanied by fibrillary twitching and partial reaction of degeneration in the muscles affected, the weakness that follows the atrophy, the bilateral localization of the atrophy in groups of muscles according to the several types that I have mentioned, and the absence of sensory disturbances (with the exception, occasionally, of pain in the muscles affected), you will rarely have difficulty, when a patient afflicted with the disease presents himself to you for examination, in arriving at a positive diagnosis of progressive (central) muscular atrophy. Beginners may make the mistake of confusing progressive (central) muscular atrophy with syringomyelia, with hematomyelia, or with the residues of a Heine-Medin disease, especially when the Aran-Duchenne type of atrophy presents itself. But in the patient before us there are no sensory disturbances that point to syringomyelia or to hematomyelia and there is no history of poliomyelitis.

There is no history of syphilis in this patient; the Wassermann test is negative; the cerebrospinal fluid has been examined and is normal. It is very easy, therefore, to rule out a luetic myelitis and a luetic meningomyelitis, conditions that may sometimes give rise to a syndrome not unlike that before us. I need scarcely dwell on the differential diagnosis as regards tumor of the spinal cord, peripheral neuritis, or multiple sclerosis. None of these diseases is likely to be confused with the progressive (central) muscular atrophy in the present instance, even by a neurologic novice.

From what I have already told you of the localization of the process in progressive (central) muscular atrophy according to types, you will have no difficulty in recognizing that this patient, though presenting a spinal form, does not exhibit the classic Aran-Duchenne type nor the Werdnig-Hoffmann type. The localization and mode of extension do conform, however, to what is known as the Vulpian-Bernhardt subvariety of the Aran-

Duchenne type, and I have, therefore, no hesitation in nosologically so placing the case.

Treatment.—I wish I had something of value to contribute toward the treatment of this malady. That we shall some time be able to cope with it, probably in a preventive way, I confidently hope. The disease seems to depend upon some toxic degenerative process, but its etiology is still entirely obscure. In our ignorance we must rely upon: (1) the removal of any toxic or infectious foci that we can find in the body, (2) upon general upbuilding measures, and (3) upon rest to the locomotor system. Two methods of pharmacotherapy have been recommended: (1) Hypodermic injections of nitrate of strychnin daily for a time, and (2) hypodermic injections of cacodylate of soda, the latter for its general "tonic" effects. The patient should be warned against all violent forms of therapy, and especially against vigorous massage, manipulations, extremes of hydrotherapy, and strong electric treatments. They only do harm; though, unfortunately, many patients, unwilling to accept the verdict of the experienced clinician, seek out more ignorant practitioners or quacks, who expect, and sometimes promise, benefit from them.

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CLINIC OF DR. HERMAN O. MOSENTHAL

JOHNS HOPKINS HOSPITAL

ESSENTIAL HYPERTENSION

A Patient Illustrating the Uncomplicated Disease and its Benign Symptomless Course. Hypertension in Many Cases is not Associated with a Nephritis. Other Patients who Demonstrate Secondary Arteriosclerotic Changes in the Aorta and Coronary Vessels, the Cerebral Arteries, and in the Blood-vessels of the Kidneys.

THIS morning I wish to take up certain phases of the subject of hypertension. The conception of hypertension as a probable symptom of Bright's disease is held by many physicians. It is far from valid, however, for many of the cases with increased blood-pressure have no lesions in the kidneys, or only those that are frequently found in individuals dying of causes not related to renal disease. In many of these cases no cause for the hypertension can be found, and the name "essential hypertension" is given to this condition. It has also been called "benign essential hypertension," as advocated by Volhard and Fahr, because of the long, often symptomless course of the disease. Dr. Janeway prefers to call it"primary hypertensive cardiovascular disease." All these, as well as many other terms, describe a symptom and are an indication of our lack of knowledge concerning its etiology.

CASE I.—The first patient is a girl eighteen years old, an employee in a candy factory. She entered the hospital eight months ago, on August 25, 1916. At that time her chief complaint was headache and pains in her stomach. Her family history is negative. The past history is singularly devoid of important occurrences. Except for measles and whooping-cough she has

had no illnesses. She eats much candy and has a great deal of thirst. Four weeks before being admitted to the hospital she went on a picnic to Bay Shore. The next day she was very weak and fainted. She worked during the following week and then discontinued her occupation because of malaise. There were pains in the head, back, and legs, and she believes that she had fever for one week. The headaches were so severe that an ice-cap was necessary. There was nycturia.

There was no fever during her stay in the hospital. Her symptoms were evidently in large part due to acute gastritis induced by indiscretions at the picnic. All complaints disappeared shortly after her entrance into the ward, and she was of interest mainly because of the discovery of certain facts on physical examination. This was negative except for the cardiac and blood-pressure findings. The examination of the heart revealed then, as it does now, a distinctly lifting impulse at the apex, a slight enlargement to the left, an aortic second sound which is markedly accentuated, and a presystolic gallop-rhythm. The blood-pressure was 210 systolic and 140 diastolic on admission, and many subsequent examinations have shown no change. In this patient, therefore, there is a hypertension, a cardiac hypertrophy, some dilatation of the left ventricle, and a slight disturbance in the heart's action. These cardiac signs are among the almost invariable sequelæ of hypertension. It is only rational to expect that an increased resistance in the general circulation should result in cardiac hypertrophy and dilatation. A presystolic gallop-rhythm and frequently also extrasystoles accompany the functional and degenerative changes occurring in the heart muscle. These may persist for long periods and are not in themselves bad prognostic signs.

Because of the presence of the increased blood-pressure the condition of the kidneys has been thoroughly investigated. A trace of albumin was found at times, and during the first few days of her stay in the hospital a few hyaline casts. These subsequently disappeared. The specific gravity of the urine, as observed in the daily examinations, was constantly low, varying between 1013 and 1005. Such a urine would correspond to a

marked degree of nephritis. Further examination, however, revealed the fact, as shown by the results of the test-meal for renal function as given on the board (Table I), that the specific gravity of the urine surpassed the usual low figure when water was withheld. This was done at night during the test-meal, and, as you see, the specific gravity rose to 1021. The urine volume at night likewise became small, measuring only 295 c.c., which is well within the normal limits. The polyuria during the daytime and the low specific gravity were due to the fact, as brought out by closer questioning, that this patient was in the habit of eating a great deal of candy and consequently drinking very much water. When water was omitted at night, the specific gravity was raised to the figure mentioned. The other tests for renal function were equally satisfactory. The phenolsulphonephthalein was tried on two occasions, and during two hours 66 and 69 per cent. of the drug were eliminated. The figure for Ambard's constant was 0.081. The urea nitrogen of the blood was 20 mg. per 100 c.c. All these tests, as you see, are perfectly normal, with the possible exception of a slight increase in the urea nitrogen of the blood. It is worthy of note that in this individual there was no arteriosclerosis of any of the palpable blood-vessels or of the retina, and that the hemoglobin and red blood-cells were not diminished, the hemoglobin being 91 per cent. and the red cells 4,664,000. The absence of an anemia goes very far toward eliminating a diagnosis of severe nephritis.

Since her discharge from the hospital this patient has been observed in the dispensary, and has continued a life free from mishaps, although her blood-pressure remains high, in the neighborhood of 200, and as you see her today she appears in perfect health and has no complaints. Her headaches have not recurred, her appetite is good, and, with the exception of lying down for two hours every afternoon, she has limited her activities in no way whatsoever. In this case no cause for the hypertension could be discovered in the kidneys, blood-vessels, or elsewhere, and hence we are justified in making the diagnosis of essential hypertension. Her diet has not been limited qualita-

tively, since we have found, after considerable investigation of this problem, that the lowering of protein food, which is so popular a remedy for this condition, does not bring down the blood-pressure, but that the best means of reducing it is to give the patient as much rest as possible. Accordingly, we reduce their activities to prevent both mental and physical overexertion, and we limit their diets quantitatively, so that they will not overdistend their stomachs nor throw an unnecessary burden on their circulation through the digestion and absorption of an excess of food.

TABLE I

TEST-MEAL FOR RENAL FUNCTION

Name: *Case I.* Date: *October 5–6, 1916.*

Time of Day.	C.c.	Sp. Gr.	NaCl. Per Cent.	NaCl. Gm.	N. Per Cent.	N. Gm.
8–10	430	1007	0.32	1.38	0.26	1.12
10–12	320	1008	0.52	1.66	0.34	1.09
12– 2	285	1009	0.42	1.20	0.37	1.05
2– 4	250	1010	0.48	1.20	0.49	1.23
4– 6	156	1013	0.52	0.86	0.61	0.95
6– 8	365	1005	0.20	0.73	0.33	1.20
Total day	1806	....	....	7.03	....	6.64
Night, 8–8	295	1021	1.06	3.13	1.11	3.27
Total, 24 hours	2101	....	....	10.16	....	9.91
Intake	1760	....	....	8.50	....	13.40
Balance	−341	....	....	—1.66	....	+3.49

Impression: Normal result. Note the increased specific gravity and high concentration of salt and nitrogen in the night specimen. The polyuria and low concentration of the day specimens may be due to the excess of candy which the patient is in the habit of taking.

Table I: Results of the test-meal for renal function in Case I.

Case II.—The course which many of these cases follow is a remarkably favorable one, as the name "benign hypertension," previously referred to, indicates. The chart on the board shows you the non-progressive type of the disease as it may occur in some individuals (Table II). Summarizing the history of this

second patient, we note that he is seventy-one years old at the present time. In 1906 he presented himself for examination to Dr. Theodore Janeway for a minor ailment. The discovery of a blood-pressure of 250 systolic and 150 diastolic was an accidental finding. Here, as in the previous case, a high blood-pressure was not accompanied by subjective symptoms. In 1891 he had a slight attack of gout of the big toe, and for a number of years "dead finger ends" after a cold bath in the morning and occasionally on exposure to cold air. He subsequently had other attacks of gout in 1908 and 1911. You will see from the record (Table II) that his blood-pressure diminished somewhat on restricting his activities, the systolic pressure going down to the neighborhood of 200, but not falling much below that point for the period of eleven years that he has been under observation.

TABLE II

Date.	Blood-pressure— Systolic.	Diastolic.	Remarks.
Dec. 10, 1906	250	150	
Feb. 2, 1907	200	120	
Mar. 3, 1907	185	110	
Jan. 23, 1908	210	130	
May 20, 1908	225	140	
Nov. 5, 1908	200	130	
Jan. 6, 1909	190	110	
Oct. 18, 1908	205	105	Aortic diastolic murmur heard for the first time.
Jan. 6, 1910	190	115	
Mar. 4, 1912	185		
Dec. 18, 1912	195		
Nov. 25, 1914	220	117	
Nov. 24, 1915	215	105	Wassermann reaction negative. Ambard's constant 0.101. Blood urea nitrogen 20 mg. per 100 c.c. Transient attacks of myocardial insufficiency.
Oct. 13, 1916	205	120	Phthalein, 40 per cent. in two hours. Blood urea nitrogen 18 mg. per 100 c.c.
Mar. 15, 1917	220	150	Auricular fibrillation; a moderate degree of myocardial insufficiency.

Table II: Data of Case II.

There are several secondary effects that may be brought about by the constant high blood-pressure. The peripheral blood-vessels become sclerosed and cause various symptoms according to their location. There are three situations in which the arteriosclerosis is most often found. These are the aorta and the coronary vessels, the cerebral and the renal arteries.

In this case in 1909 a diastolic murmur was noted over the aortic area for the first time by Dr. Janeway. Evidently there was an arteriosclerosis of the aorta resulting in a deficiency of the aortic valves. This murmur has persisted ever since and has become louder. The patient's Wassermann reaction was negative, and evidently his aortic insufficiency should not be ascribed to syphilis.

During the later period of observation it was possible to test his renal function, and, as you see on the chart (Table II), his phenolphthalein excretion indicated only a slightly diminished renal function; this was the case also with the blood urea and the Ambard constant. Finally, after ten years of persistent high blood-pressure of which we know, and possibly for many years of which we have no record, this individual began to show symptoms referable to his heart. In October, 1916, numerous extrasystoles appeared, associated at that time with transient attacks of myocardial insufficiency. Subsequently auricular fibrillation manifested itself. It would seem, therefore, that this man is approaching the end of life, and in a manner which is very common in cases of hypertension—namely, with a myocardial insufficiency. The heart in these cases is no longer able to cope with the strain to which it is put and heart failure is the result. One factor concerning these patients is remarkable. The myocardial insufficiency is much more likely to be amenable to treatment than in cases of endocarditis. The dyspnea, edema, cardiac palpitation, etc., may manifest themselves a very long time before the symptoms become so severe as to seriously interfere with a moderately active life. Here again we see a reason why this form of hypertension has been described as benign.

Case III.—I wish to call your attention to a third case of essential hypertension which illustrates a secondary involve-

ment of another set of arteries—namely, those of the brain. A postmortem examination was performed on this patient last fall, so that all I can do is to give you the history and show you the lantern slides which were made by Drs. Adolf Meyer and Admont Clark from the autopsy material. The history is well worth considering.

This patient was forty years old, a lawyer, a native of the United States. There was catarrhal jaundice in 1901. In July, 1909, a diagnosis of "intestinal putrefaction, overwork, and intoxication due to bacterial activity and hepatic insufficiency" was made by a prominent New York physician. The data on which this diagnosis rested were as follows: "Eight years ago the patient worked hard, was under considerable nervous strain, and began to have digestive attacks with fever, pain in the legs and abdomen. One of these attacks ended with catarrhal jaundice, lasting four to five weeks." Similar attacks, but without nausea, vomiting, or pain, have occurred since July, 1909. At this time the physical examination was negative except for poor nourishment and pale mucous membranes; there were no blood-pressure readings. In May, 1910, a New York consultant reversed the opinion given one year previously by his colleague and made a diagnosis of "hyperacidity."

On May 20, 1910, there was "specky" darkness in the lower half of vision; a short time later the eyes were suddenly drawn to the left, the patient became unconscious and remained so for half an hour; a diagnosis of uremia was made. Subsequently, severe occipital headaches set in. From 1913 on there was a considerable diminution in his working power.

The final illness dated from November, 1915, when the headaches became very much intensified and never left him completely. The systolic blood-pressure varied between 190 and 255. There were several attacks of complete unconsciousness, in each one the patient being revived by bleeding. On several occasions there was transient motor aphasia, with some weakness of the right side of the face. No other palsies were noted. There was a great deal of vomiting, and at intervals there were convulsive seizures. He finally lapsed into a condition of com-

plete unconsciousness; it was impossible to administer nourishment, and he died in October, 1916.

The physical examination, except for the high blood-pressure and the poor nourishment alluded to above, yielded remarkably little. The mucous membranes were pale. There was no thick-

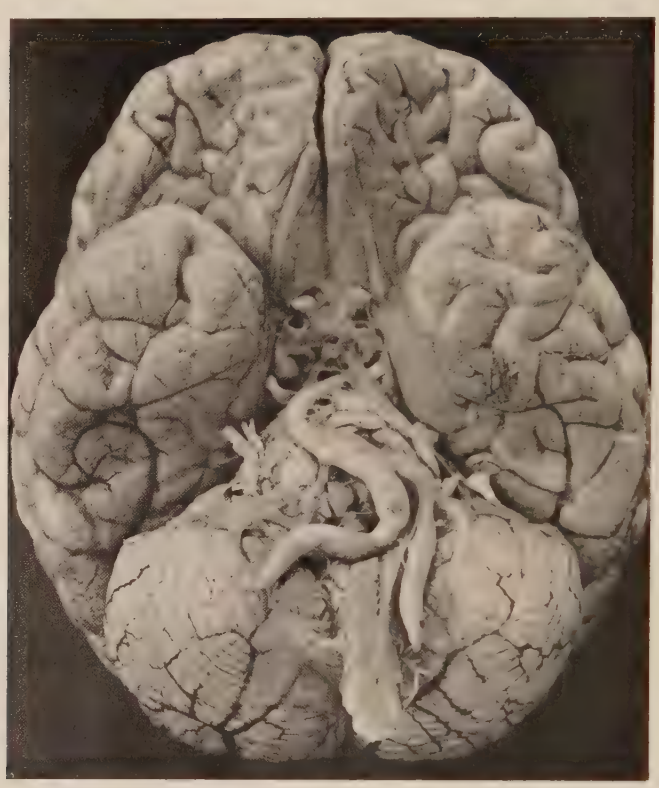

Fig. 9.—Base of the brain of Case III. The vertebral and basilar arteries are very tortuous and irregular in outline. The right vertebral artery compresses the medulla oblongata (Dr. Adolf Meyer).

ening of the vessels; no increase of retromanubrial dulness, indicating a dilated aorta. The eyes reacted to light; an ophthalmoscopic examination was impossible because of an extreme degree of myopia. The knee-jerks were present. The heart was normal except for evident enlargement to the left; there were no murmurs. The Wassermann test done some time pre-

viously was negative. The phenolphthalein test varied between 44 and 61 per cent. in two hours. The non-protein nitrogen of the blood varied between 31 and 38 mg. Ambard's coefficient was normal (78, McLean's index). The urine showed a trace of albumin and an occasional hyaline or granular cast. The specific gravity varied between 1010 and 1017.

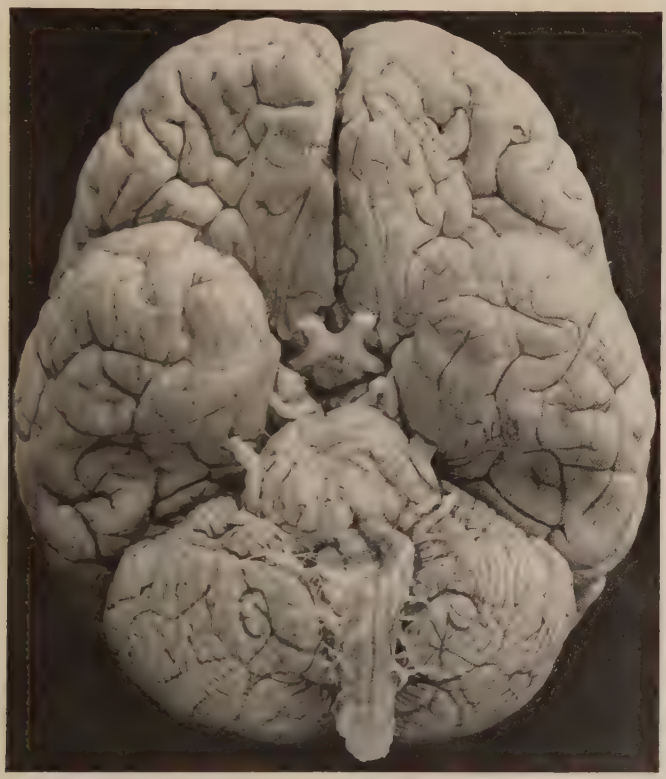

Fig. 10.—Base of the brain of Case III after removal of the arteries. The depression caused by the pressure of the right vertebral artery on the medulla oblongata is plainly seen (Dr. Adolf Meyer).

It is evident that in this case we are dealing with hypertension, and here, as in the preceding cases, we are confronted with only a minimal involvement of renal function. The diagnosis of uremia, therefore, in the final attack, or in the previous at-

tacks, is entirely unwarranted. At the present time we are able to make our diagnosis from the autopsy findings, and we

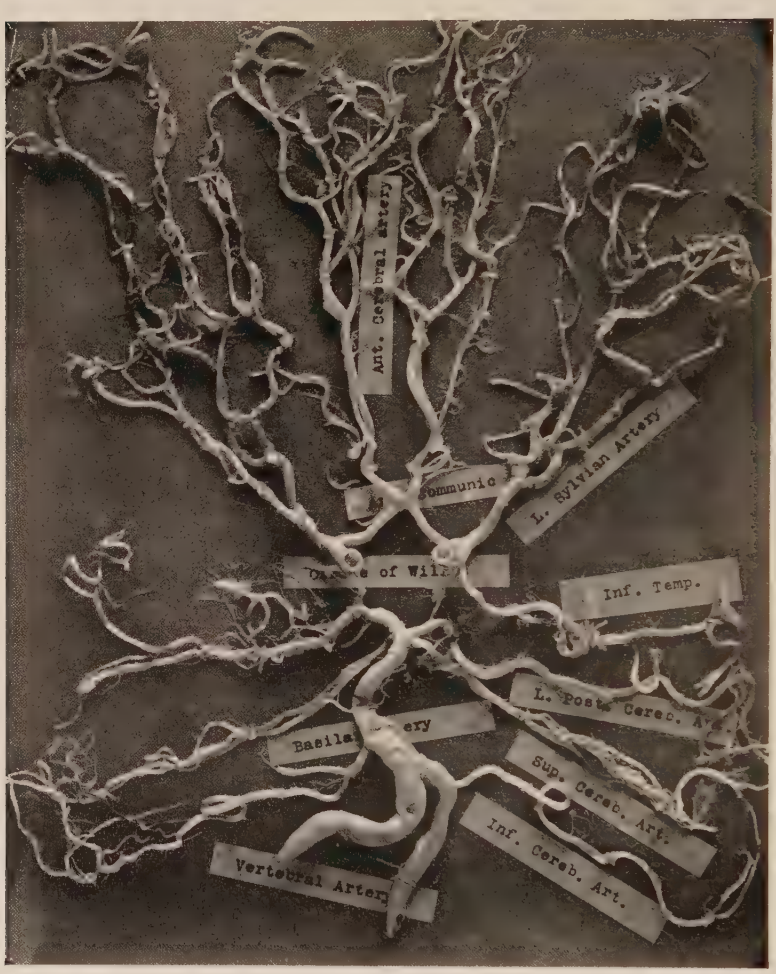

Fig. 11.—The cerebral arteries after removal from the brain of Case III. The vessels are extremely tortuous and irregular in outline. Some arteries are markedly dilated; others, as the posterior communicating branches of the circle of Willis, are almost obliterated (Dr. Adolf Meyer).

know that the sclerosed condition of the vessels of the brain was probably responsible for most of the very varied gastro-

intestinal and cerebral symptoms which have been detailed to you.

The picture on the screen shows the base of the brain (Fig. 9). The vertebral and basilar arteries are very tortuous and irregular in their outlines. In becoming distorted in this fashion the vessels have pressed upon the surrounding brain tissue, as you see in the next photograph (Fig. 10), which shows the base of

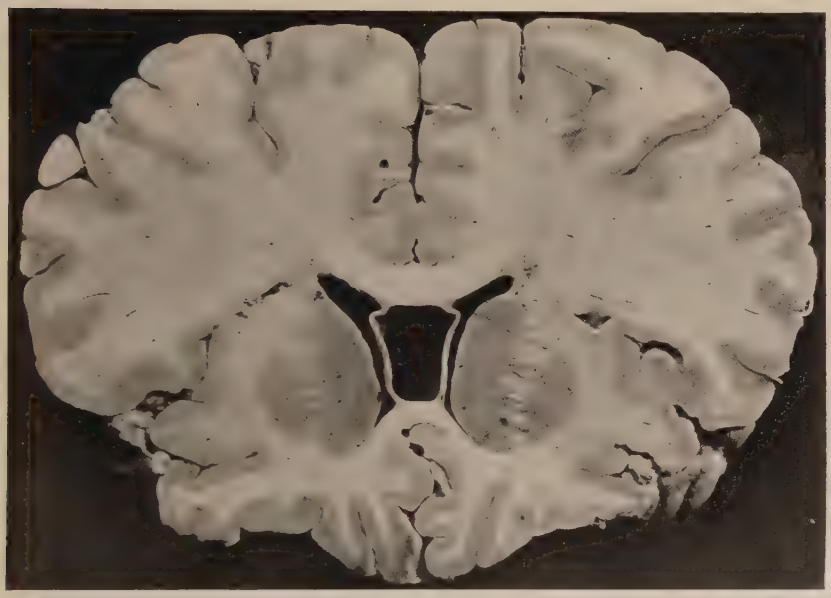

Fig. 12.—Cross-section of the brain from Case III. There is a considerable number of small hemorrhages and areas of softening. This section was chosen because it shows one larger lacuna of softening in the left internal capsule which was responsible for the aphasia and weakness of the right side of the face (Dr. Adolf Meyer).

the brain after the removal of the blood-vessels. We note that the medulla has been compressed in its upper part to about a third of its depth. Such pressure on the medulla oblongata might account for the gastro-intestinal disturbances, as well as the so-called attacks of uremia. The very beautiful preparation of the vessels of the base of the brain (Fig. 11) which Dr. Meyer has furnished us demonstrates a remarkable condition. Not

only the basilar and vertebral arteries, as we saw in one of the previous pictures, are dilated and tortuous, but all of the cerebral arteries are more or less involved in the same arteriosclerotic process. Of particular interest are the posterior communicating arteries of the circle of Willis, which are almost obliterated.

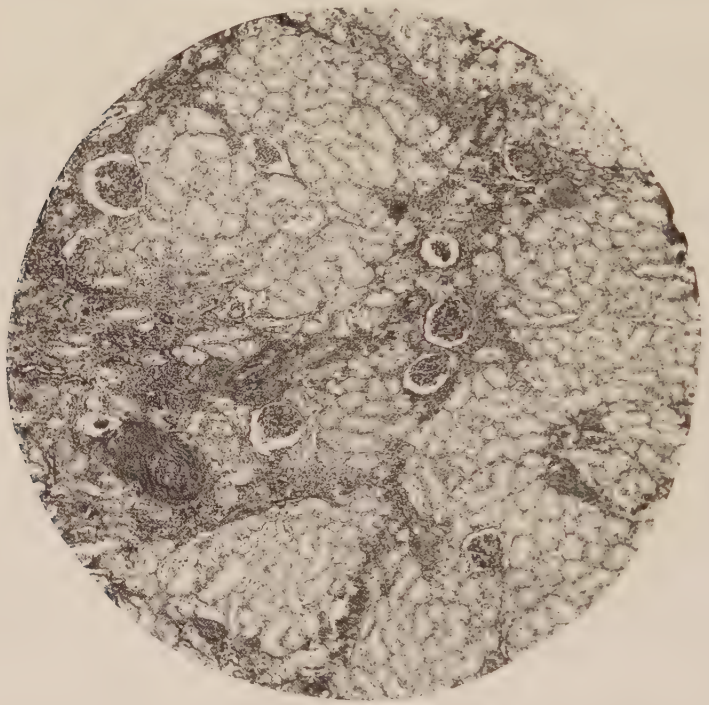

Fig. 13.—Kidney from Case III. Area of maximal renal involvement. Vascular type of nephritis of slight degree. The blood-vessels are thickened. Several hyalinized glomeruli are seen in the upper right-hand corner of the field. There are areas of round-cell infiltration. The greater portion of the kidney tissue is normal in appearance (Dr. Admont Clark).

Taking these extreme arterial changes in the peripheral cerebral arteries into consideration, it is only to be expected that those branches which penetrate the brain itself have not escaped involvement. In the next picture (Fig. 12) the lacunæ of softening brought about by insufficient blood flow through the narrowed vessels and the hemorrhages occurring because of the weakened

arterial walls may be noted. Similar changes were found throughout the whole brain. One lesion in this picture (Fig. 12) deserves particular comment. In the upper part of the left internal capsule is seen an area of softening larger than the rest. This was responsible for the motor aphasia and the weakness of the right side of the face.

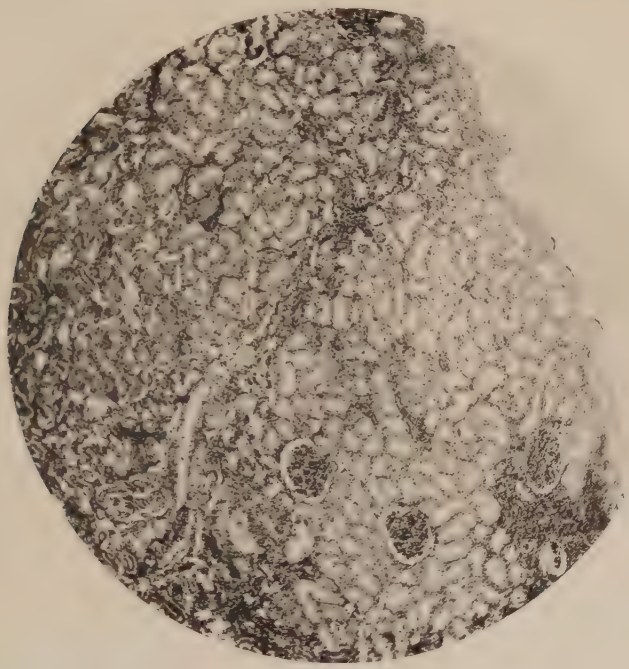

Fig. 14.—Kidney from Case III. This represents the condition of the greater portion of the tissue. Except for the small areas of round-cell infiltration, there is no lesion. The glomeruli and tubules are normal in appearance, and evidently the vascular changes have resulted only in a minimal degree of nephritis (Dr. Admont Clark).

This case is a very beautiful example of cerebral arteriosclerosis, presumably secondary to hypertension, in which the remainder of the body is free from arterial or other disease. The sections of the kidney (Figs. 13, 14) show that there is a very slight patchy sclerosis of the renal vessels, small areas of round-cell infiltration, and occasional hyalinized glomeruli, but that

the greater portion of the kidney tissue is apparently in normal condition, and certainly not in a state to induce uremia. The clinical symptoms which were identical with those of uremia are in this case to be ascribed to the cerebral arteriosclerosis. During life the correct diagnosis was made because the renal functional tests showed little or no involvement of the kidneys. The cerebral irritation, therefore, was not due to the deranged metabolism accompanying Bright's disease, but to the cerebral arteriosclerosis.

Case IV.—Finally, I wish to bring this case to your attention. The history is as follows: The patient is fifty-nine years old, his occupation that of traveling salesman. He was first admitted to the hospital about one year ago, on April 10, 1916. His chief complaint was "weakness and high blood-pressure." He also had some urinary disturbance, which, to anticipate his physical examination, was secondary to hypertrophy of the prostate gland. The history of one year ago states that his present illness began three years before, in 1913, when he felt restless, nervous, and weak. The systolic blood-pressure varied between 220 and 240. He has felt particularly weak in the legs and his left leg has been numb. The physical examination at that time showed some anemia, an area of precordial dulness, extending 12 cm. to the left and 3 cm. to the right, a presystolic gallop-rhythm, and an occasional extrasystole. The radial, brachial, posterior tibial, and dorsalis pedis arteries were thick and tortuous. The ophthalmoscopic examination was negative; there were no hemorrhages, areas of exudate, or signs of arteriosclerosis in the retinal vessels. The blood-pressure was 190 systolic and 130 diastolic. A rectal examination revealed a large and firm prostate.

At that time this case presented the picture which we have already noted. Hypertension, resulting in cardiac hypertrophy and dilatation, a presystolic gallop-rhythm, and occasional extrasystoles. The arteriosclerosis of the palpable peripheral vessels is more in evidence in this patient than in the previous ones. The weakness in both legs and the numbness in the left leg point to the possible narrowing of the blood-vessels and poor

circulation in the lower limbs. In this patient the course of the tests for renal function was of extreme interest. One year ago they were found to show only a slight impairment of renal efficiency. Ambard's constant was 0.065. The urea nitrogen was 10 mg. per 100 c.c. The excretion of phenolsulphonephthalein was somewhat diminished, being 40 per cent. in two hours, and the test-meal for renal function revealed a slight impairment, as shown by the rather low specific gravity, the maximum being 1015 instead of 1018, and a distinct nocturnal polyuria (Table III). The first two tests are well within the normal limits, while the last two show a slight impairment of renal function. This is surely not a condition indicating an alarming degree of kidney insufficiency.

TABLE III

TEST-MEAL FOR RENAL FUNCTION

Name: *Case IV.* Date: *April 14–15, 1916.*

Time of Day.	C.c.	Sp. Gr.	NaCl. Per Cent.	NaCl. Gm.	N. Per Cent.	N. Gm.
8–10	385	1007				
10–12	112	1014				
12– 2	178	1013				
2– 4	136	1015				
4– 6	176	1015				
6– 8	226	1009				
Total day	1213	....	0.34	4.12	0.55	6.67
Night, 8–8	622	1013	0.58	3.61	0.58	3.61
Total 24 hours	1835	....	....	7.73	....	10.28
Intake	1760	....	....	8.50	.. ..	13.40
Balance	−75	....	....	+0.77	....	+3.12

Impression: Low specific gravity (maximum is 1015 instead of a normal of 1018). Variation of specific gravity is 8 degrees (normal 9 degrees). A slight but distinct nocturnal polyuria. A moderate impairment of renal function.

Table III: Results of the test-meal for renal function in Case IV one year ago.

TABLE IV

TEST-MEAL FOR RENAL FUNCTION

Name: *Case IV.* Date: *April 25–26, 1917.*

Time of Day.	C.c.	Sp. Gr.	NaCl. Per Cent.	NaCl. Gm.	N. Per Cent.	N. Gm.
8–10	77	1012				
10–12	85	1011				
12– 2	69	1013				
2– 4	71	1012				
4– 6	61	1011				
6– 8	80	1011				
Total day	443	....	0.24	1.06	0.50	2.22
Night, 8–8	595	1010	0.25	1.48	0.42	2.49
Total 24 hours	1038	....	....	2.54	....	4.71
Intake	1610	....	....	6.50	....	12.00
Balance	+572	....	....	+3.96	....	+7.29

Impression: Marked fixation of the specific gravity at a low level. A maximal impairment of renal function.

Table IV: Results of the test-meal for renal function in Case IV at the present time.

One year ago, therefore, there was a hypertension of more than three years' standing in a patient who was not suffering seriously from this disease. Today there is an entirely different picture. The patient complains of severe occipital headaches. After leaving the hospital he felt well until four months ago, when the headaches began. They frequently awaken him at night, when they may be severe; to use his own words, they are "general and thumping in character." About five months ago the patient fainted and remained unconscious for two hours. One month ago he had an attack of vertigo lasting two hours. This, as well as the previous attack, cleared up without leaving any weakness or residual paralysis. Some dyspnea began four months ago. This comes on at night and is relieved by sitting up in bed. These attacks resemble asthma in their characteristics. They are, doubtless, signs of myocardial insufficiency.

From what we have observed in the previous cases, we may well suspect cerebral arteriosclerosis in this patient. However,

we must not forget that the symptoms may likewise be associated with insufficient kidney action, and that in these cases we have no measure of the kidney condition except by the tests for renal function. In this case, on repeating the tests which we had done about one year previously, we find a totally different state of affairs. His test-meal for renal function shows a change from a condition of variable specific gravity to one in which the specific gravity is remarkably fixed, remaining at a level of about 1010, the maximum variation being 1 degree in either direction from this point. This would enable us to say that the renal involvement has progressed considerably since the last examination, and, as far as this test is concerned, there is a maximal involvement of renal function (Table IV). The other functional tests reveal an equally marked change from the condition of a year ago. The blood urea nitrogen is 79 mg. per 100 c.c. Ambard's constant is 0.47, and the phenolphthalein is only a trace in two hours. Evidently in this patient the vascular lesions in the kidney have progressed very rapidly and only a minimal amount of functionating renal tissue remains. Here, therefore, we have the third of the common sequelæ of essential hypertension, the others being, as we have seen, sclerotic changes in the aorta and in the cerebral vessels. It thus becomes apparent that although some of these patients have a long life and a remarkably uneventful one, this is not always the case. It seems to be largely a matter of chance, depending, in the first place, upon the extent of secondary arteriosclerotic degeneration, and, in the second place, upon the site of such changes. The particular arteries involved may or may not supply vitally necessary organs.

The treatment in all of these cases is approximately the same: as much mental and physical rest as is possible and a symptomatic treatment for myocardial insufficiency, renal insufficiency, or disease of other organs, should their involvement require it. No cure is at present within reach; the hypertension cannot be successfully combated with drugs, but only by relieving the stress and strain of daily life.

THE DIETETIC TREATMENT OF DIABETES MELLITUS

A List of Diets which are Easily Handled by the Nurse or Patient and the Physician. The Importance of Avoiding an Excess of Fats. The Necessity of Rendering the Urine Free from Sugar on a Diet of Sufficient Caloric Value to Maintain the Health and Strength of the Individual. This is Best Accomplished by a Carbohydrate-free Diet of 1500 to 1700 Calories and the Subsequent Addition of Starchy Food. A Patient Illustrating These Principles of Treatment.

THIS patient is thirty-eight years old, an engineer, a native of Maryland. He presents himself complaining of marked loss of weight and strength. Two years ago he suffered from great thirst, a very large appetite, and frequent urination. At that time his physician examined his urine and found a marked reaction for glucose. He has systematically neglected all treatment and has steadily lost weight and strength until the condition in which you see him has been brought about. He now weighs 100 pounds, whereas two years ago he weighed 182 pounds. The emaciation is very evident. The skin is dry and there have been several large furuncles over various parts of his body, a few of which still remain.

There is no doubt about the diagnosis. We are dealing with a case of diabetes mellitus in which the dietetic treatment has been neglected and the patient has consequently done very poorly. At the present time, as you know, we attempt virtually no drug therapy in this condition, but treat the disease principally by dietetic means. In the dietetic treatment of this disease our aim is to eliminate the sugar from the urine, to bring the blood-sugar back to a normal level, to do away with the dangers of acidosis, and at the same time to attempt to maintain the individual's health and strength. This morning I should like to give

you a summary of the method which we use in the hospital to obtain our object.

The diet lists which I am passing around are those we use in the treatment of these cases in the wards. In the first place we have the starch-free list (Table I), which enumerates the foods with a minimum quantity of starch that we allow patients to take while they are on a so-called "carbohydrate-free diet."

TABLE I

STARCH-FREE DIET

May eat:

Soups: Clear meat broths.

Meats: All kinds of meat, fresh, smoked, or cured, except liver; all meats must be prepared without flour or breadcrumbs.

Fish: All kinds of fish, but no clams, oysters, or scallops.

Eggs: Eggs in any form, prepared without milk, flour, or sweetening (sugar, jam, etc.).

Butter: Butter, oil, and lard.

Cheese: All kinds of cheese.

Vegetables: Greens, spinach, string-beans, Brussels sprouts, asparagus, kohl-rabi, rhubarb, egg-plant, water-cress, lettuce, endive, cucumbers, celery, cabbage, mushrooms, tomatoes, sour pickles, sauerkraut, sorrel, Swiss chard, cauliflower.

Gluten products: "Akoll" biscuits.

Desserts: Gelatin jellies (use sour white wine, brandy, or coffee for flavoring).

Beverages: Tea and coffee, sweetened with saccharin (without sugar or milk); claret, burgundy, sour white wine, and whisky in moderate amounts. Vichy and water.

Condiments: Pepper, salt, mustard, oil, vinegar.

Must avoid eating:

Sugar in any form. Bread, biscuits, and cakes of all kinds. Toast, crackers, rice, oatmeal (and all cereals); sago, tapioca, macaroni, vermicelli, potatoes, carrots, parsnips, beets, corn, beans, peas. All fruits: fresh, preserved, and dried. Jams and jellies. Pastry, puddings, and ice-cream. Sauces and gravies thickened with flour.

Must avoid drinking:

Milks, ales, porter, stout, beer, cider, all sweet wines, port wine, liqueurs, sparkling wines, syrups.

In certain cases this diet alone accomplishes our object. It renders the urine sugar free and enables the patient to do very

well even without going to the trouble of weighing the food. However, there are some individuals in whom this diet will not have the desired results. In these the source of glucose must be sought in the proteins as well as in the carboyhydrates, and it is obvious that an individual taking food from this list without restriction is likely to take so much protein that glucose may appear in the urine. We, therefore, have designed another series of lists of carbohydrate-free diets, varying from 500 to 2000 calories, in which not only the kind of food but its quantity as well is specified (Tables II, III, IV, V, and VI).

TABLE II

CARBOHYDRATE-FREE DIET, 500 CALORIES

Food.	Gm. or C.c.	Protein, Gm.	Fat, Gm.	C–H, Gm.	Calories.	Calories per Meal.
Breakfast:						
One egg	50	6.6	6.0	0	83	
Bacon[1]	40	4.2	7.6	0	88	
Black coffee	...	..	..	..	..	171
Dinner:						
Broth	150	3.3	0.3	0	16	
Steak[2]	40	9.4	4.1	0	77	
Vegetables[3]	200	2.0	0	6.0	33	
Butter	5	0.1	4.3	0	40	
Black coffee	...	..	..	..	..	166
Supper:						
Broth	150	3.3	0.3	0	16	
Steak[2]	40	9.4	4.1	0	77	
Vegetables[3]	200	2.0	0	6.0	33	
Butter	5	0.1	4.3	0	40	
Plain tea	...	..	..	..	..	166
		40.4	31.0	12.0	...	503

[1] The bacon is weighed uncooked. The fat and protein content is calculated for the cooked product.

[2] The caloric equivalent of other carbohydrate-free meat or fish should be frequently substituted from the accompanying list, to furnish variety in the diet.

[3] Two or three different vegetables should be chosen from the accompanying list, which tabulates the vegetables containing 5 per cent. or less of carbohydrates.

TABLE III

CARBOHYDRATE-FREE DIET, 1000 CALORIES

Food.	Gm. or C.c.	Protein, Gm.	Fat, Gm.	C–H, Gm.	Calories.	Calories per Meal.
Breakfast:						
Eggs (2)	100	13.2	12.0	0	166	
Bacon[1]	50	5.3	9.6	0	111	
Butter	5	0.1	4.3	0	40	
Black coffee	...	..	..	..	..	317
Dinner:						
Broth	150	3.3	0.3	0	16	
Steak[2]	100	23.9	10.2	0	193	
Vegetables[3]	200	2.0	0	6.0	33	
Olive oil	10	0	10.0	0	93	
Butter	10	0.1	8.6	0	80	
Black coffee	...	..	..	..	..	415
Supper:						
Broth	150	3.3	0.3	0	16	
Steak[2]	75	17.9	7.7	0	145	
Vegetables[3]	200	2.0	0	6.0	33	
Butter	10	0.1	8.6	0	80	
Tea (plain)	...	..	..	..	..	274
		71.2	71.6	12.0	..	1006

TABLE IV

CARBOHYDRATE-FREE DIET, 1500 CALORIES

Food.	Gm. or C.c.	Protein, Gm.	Fat, Gm.	C–H, Gm.	Calories.	Calories per Meal.
Breakfast:						
Eggs (2)	100	13.2	12.0	0	166	
Bacon[1]	60	6.4	11.5	0	133	
Butter	10	0.1	8.6	0	80	
Black coffee	...	..	..	..	..	379
Dinner:						
Broth	150	3.3	0.3	0	16	
Steak[2]	140	33.5	14.3	0	270	
Vegetables[3]	200	2.0	0	6.0	33	
Cream cheese	20	5.2	6.7	0.5	86	
Olive oil	15	0	15.0	0	140	
Butter	15	0.2	12.9	0	120	
Black coffee	...	..	..	..	..	665

[1] The bacon is weighed uncooked. The fat and protein content is calculated for the cooked product.

[2] The caloric equivalent of other carbohydrate-free meat or fish should be frequently substituted from the accompanying list, to furnish variety in the diet.

[3] Two or three different vegetables should be chosen from the accompanying list, which tabulates the vegetables containing 5 per cent. or less of carbohydrates.

Food.	Gm. or C.c.	Protein, Gm.	Fat, Gm.	C–H, Gm.	Calories.	Calories per Meal.
Supper:						
Broth	150	3.3	0.3	0	16	
One egg	50	6.6	6.0	0	83	
Steak[1]	100	23.9	10.2	0	193	
Vegetables[2]	200	2.0	0	6.0	33	
Butter	15	0.2	12.9	0	120	
Tea (plain)	...	..	..	..	..	445
		99.9	110.7	12.5	..	1489

TABLE V

CARBOHYDRATE-FREE DIET, 2000 CALORIES

Food.	Gm. or C.c.	Protein, Gm.	Fat, Gm.	C–H, Gm.	Calories.	Calories per Meal.
Breakfast:						
Eggs (2)	100	13.2	12.0	0	166	
Ham	75	15.2	16.8	0	219	
Butter	15	0.2	12.9	0	120	
Vegetables[2]	100	1.0	0	3.0	16	
Black coffee	...	..	..	..	..	521
Dinner:						
Broth	160	3.5	0.3	0	17	
Steak[1]	160	38.2	16.3	0	308	
Vegetables[2]	300	3.0	0	9.0	49	
Cream cheese	30	7.8	10.1	0.7	129	
Butter	20	0.2	17.2	0	160	
Olive oil	15	0	15.0	0	140	
Black coffee	...	..	..	..	..	803
Supper:						
Broth	160	3.5	0.3	0	17	
Eggs (2)	100	13.2	12.0	0	166	
Steak[1]	140	33.5	14.3	0	270	
Vegetables[2]	300	3.0	0	9.0	49	
Butter	20	0.2	17.2	0	160	
Tea (plain)	...	..	..	..	..	662
		135.7	144.4	21.7	..	1986

[1] The caloric equivalent of other carbohydrate-free meat or fish should be frequently substituted from the accompanying list, to furnish variety in the diet.

[2] Two or three different vegetables should be chosen from the accompanying list, which tabulates the vegetables containing 5 per cent. or less of carbohydrates.

TABLE VI

CALORIC EQUIVALENT OF 10 GM. OF STEAK IN CARBOHYDRATE-FREE MEAT OR FISH

Food.	Gm.	Fat, Gm.	Protein, Gm.	Calories.
Steak	10	1.0	2.4	19
Roast beef	5	1.4	1.1	18
Tongue	7	1.4	1.6	20
Lamb chop	5	1.5	1.1	18
Roast lamb	8	1.3	1.6	20
Sweetbreads	11	0.1	4.4	19
Boiled ham	7	1.4	1.5	19
Fried ham	5	1.7	1.1	20
Roast pork	9	0.9	2.6	19
Bacon	9	1.7	0.9	20
Chicken	10	1.0	2.4	19
Duck	9	1.3	1.8	19
Guinea-hen	12	0.8	2.8	19
Squab	9	1.1	2.1	19
Turkey	7	1.3	2.0	20
Bluefish	13	0.6	3.5	20
Halibut	16	0.7	3.3	20
Mackerel	15	1.0	2.5	20
Sardines in oil	7	1.4	1.6	20

VEGETABLES ALLOWED ON "CARBOHYDRATE-FREE" DIET

Asparagus.	Endive.	Sorrel.
Brussels sprouts.	Greens.	Spinach.
Cabbage.	Kohl-rabi.	String-beans.
Cauliflower.	Lettuce.	Swiss chard.
Celery.	Pickles (sour).	Tomatoes.
Cucumbers.	Rhubarb.	Water-cress.
Egg-plant.	Sauerkraut.	

APPROXIMATE EQUIVALENT IN ALCOHOL OF 30 C. C. (1 OUNCE) OF WHISKY IN LIQUORS CONTAINING 2 PER CENT. OR LESS OF CARBOHYDRATE

	C.c.	Household Measure.
Gin, Rum, Brandy	30	2 tbsp.
Claret, Burgundy, Hock, Rhine, and Moselle wines	130–160	¾ tumbler.

TABLE VII

C. B.: Diabetes mellitus. Effects of diet on glycosuria and glycemia. Fasting is unnecessary in this case to render the urine sugar free, but is of great value in reducing the blood-sugar.

Date.	Urine. Volume 24 Hrs., C.c.	Glucose. Per Cent.	Glucose. Gm.	Blood-sugar, Per cent.	Diet. Protein, Gm.	Fat, Gm.	Carbohydrate, Gm.	Alcohol, C.c.	Total Calories.
Nov. 1...	3510	3.1	108.8	0.29	100	97	92	...	1689
2...	2265	4.5	101.9	...	100	106	91	...	1769
3...	2120	3.9	82.7	...	100	109	90	...	1793
4...	1630	2.3	37.5	0.29	101	105	13	...	1444
5...	1135	1.7	19.3	...	101	111	13	...	1500
6...	1300	1.7	22.1	...	94	111	13	...	1471
7...	1340	1.7	22.8	0.28	91	114	12	...	1483
8...	1445	1.1	15.9	...	71	72	12	...	1010
9...	1140	0.9	10.3	...	72	70	12	...	995
10...	1200	0.5	6.0	...	67	74	12	...	1012
11...	1400	0.4	5.6	...	72	71	12	...	1005
12...	945	0	0	0.24	71	72	12	...	1010
13...	3010	0	0	0.22	20	2	0	38	367
14...	1760	0	0	0.18	20	2	0	38	367
15...	2680	0	0	0.13	20	2	0	38	367
16...	1500	0	0	0.10	41	31	12	38	772
	(Diet 1000 to 1500 calories in interval.)								
24...	1650	0	0	0.15	114	128	13	...	1711
	(Diet 1700 calories in interval.)								
30...	1825	0	0	0.13	115	127	13	...	1706
Dec. 1...	2445	0.3	7.3	...	141	143	23	...	2002
2...	1292	0.4	5.2	0.18	142	143	22	...	2002
	(Diet 2000 calories in interval.)								
9...	1045	Trace.	...	0.17	142	143	22	...	2002
	(1 fast day, followed by 1700 calorie diet in interval.)								
15...	2560	0	0	0.07	113	125	18	...	1700

In the treatment of this individual (Table VII) we began with a diet of approximately 1500 to 1700 calories. You will note that the quantity of protein and the quantity of fat are approximately equal in these diets (Tables II to V and VII). This, as we have determined, represents the minimal amount of fat that will make the diet palatable over a long period. By using this ratio of fat to protein it is found that in most instances the acidosis is controlled, and no further attention need be paid to it. There are certain exceptions to this rule, and if the acid bodies are excreted in large amounts in the urine or the hyperpnea

characteristic of acidosis is present, it is necessary to resort to other means, which have been previously detailed to you. It is seen that after a few days of this diet the patient still had glucose in his urine. This, however, diminished from day to day, until finally, at the end of twelve days, the sugar had completely disappeared. We, therefore, have attained one of our objects in the treatment of diabetes—namely, the urine is rendered free from sugar. We know that under these circumstances the tolerance for carbohydrates will have a tendency to increase and that the patient's disease will probably not progress. There are other more drastic measures of rendering the urine free from glucose, such as the starvation method, which usually goes under the name of "Allen's treatment." Under certain circumstances the urine cannot be rendered sugar free by partial reduction of the diet, and then it is necessary to resort to starvation. However, by using diets which are low in calories and low in carbohydrates this is not necessary in every case, and much may be accomplished without resort to the more drastic dietary measures. In this case, although the urine was free from sugar, the blood-sugar was still at a high level—0.24 per cent. This blood-sugar was reduced to a normal level by means of the starvation treatment, so that in this instance we have accomplished our object by supplementing the restricted starch-free diet by starvation treatment.

Subsequently the diet was augmented, using the diets between 500 and 2000 calories, according to the lists, maintaining the same ratio of protein and fat that we had before. The object in using the diets graded as they are in Tables II to V is now apparent. The meals may be ordered with a minimum of figuring, and with a very slight amount of trouble on the part of the nurses or patients and physicians. By means of very simple calculations a diet of any caloric value may be obtained when the values of the 500 to 2000 calorie diets are at hand. The further treatment showed that with a daily food value of 2000 calories a small amount of sugar was present in the urine, and consequently, as on December 15th, the diet had to be reduced to 1700 calories.

The question now arises, How high should we raise the food value in these patients in order to give them a maintenance diet? An abstract of this case, given in Table VIII, shows you that a carbohydrate-free diet of 1700 calories, in which the proteins and fats were approximately equal to each other gram for gram, was necessary in order to procure maintenance as measured by the nitrogen balance. Therefore our object would be to bring him up to a diet of 1700 calories of the carbohydrate-free food and subsequently to add starchy material. No increase in the positive nitrogen balance was brought about by increasing the caloric value of the carbohydrate-free diet. In this case (Table VIII) the 2000 calorie diet accomplished nothing further in this direction than did that of 1700 calories.

TABLE VIII

Abstract from the data of C. B.: Diabetes mellitus; height, 5 ft. 7 in.; weight, 103 lbs.; showing the calories necessary in order to bring about maintenance on a "carbohydrate-free" diet. The standard by which maintenance is measured in this case is the nitrogen balance. The amounts of fat and protein given were approximately equal to each other, gram for gram, as in the 1000- and 1500-calorie diets already distributed. The only carbohydrate was that contained in the green vegetables. This may be considered the minimal diet on which an individual may maintain his health and strength, and the quantity of food for each patient should reach at least these proportions. The amounts necessary may vary somewhat, being either larger or smaller, according to the size of the individual. It is not necessary to increase the protein and fat content of the food when this "maintenance level" has been reached, but it is advisable to add starches if the patient's carbohydrate tolerance warrants it.

Period, Days.	Glycosuria per Day.	Nitrogen per Day. Intake.	Output (Urine and Feces).	Balance.	Carbohydrate-free Diet Calories per Day.
3	0	11.4	14.9	−4.5	1006
4	0	16.1	17.9	−1.8	1503
7	0	17.9	16.7	+1.2	1704
9	Trace.	22.2	21.6	+0.6	2003
		TWO MONTHS LATER			
9	6	15.6	16.7	−1.1	1504
5	0	10.7	14.8	−4.1	950
3	0	15.1	15.9	−0.8	1473
14	0	18.5	17.6	+0.9	1711
16	0	18.9	17.7	+1.2	1984

Of course it is impossible to carry out this rather intricate metabolism experiment on every patient. We now know, from a considerable number of observations, that in smaller individuals a 1500-calorie carbohydrate-free diet, with the proportion of proteins and fats as previously indicated, and in larger ones a 1700-calorie diet will bring about the desired result. After the patient's food intake has been brought to this level, it is not wise to augment the protein and fat content of the food, but to add starches. This is a welcome change to the diabetic, and it also is a rational procedure from the point of view of nutrition, since it is well known that the carbohydrates furnish the most economic and efficient means of conserving the body's protein tissues. In the case under consideration the diet could not be increased beyond 1700 calories, as sugar appeared in the urine (Table VII). Therefore it was impossible to order any starchy food. In suitable patients with a better carbohydrate tolerance the starches may be added slowly to the diet. Cream is usually the first article desired, then bread, and subsequently fruit. The increase should be made by the addition of 10 to 15 grams of starch every fourth or fifth day. In this manner the exact level of food intake resulting in glycosuria may be noted and suitable steps taken to check it. Table IX furnishes you with a list of foods rich in carbohydrate. This is designed to provide variety by suitable substitution for those patients who may indulge in a considerable amount of starch. All the foods are calculated both in terms of the rougher household measures and in grams or cubic centimeters as the equivalent of 30 grams (that is, 1 ounce) of white bread (representing 15 grams of starch), which is the weight of the usual slice of white bread served at our meals. As a rule it is wise, when possible, to maintain the diet in each case at a level of approximately 30 per cent. below the maximal carbohydrate tolerance, and, in addition, to order once a week a diet of a considerably restricted character. In the present case a daily ration of 1700 calories, with a 1000-calorie day once a week, was advised. In this way the possible excesses of diet which a patient may indulge in, and the results of mental and physical strain which often produce a glycosuria, may be partially obviated.

TABLE IX

DIABETES MELLITUS—THE ACCESSORY DIET OF FOODS RICH IN CARBOHYDRATES

If the patient's urine continues to be sugar free on a "carbohydrate-free" diet of sufficient caloric value, carbohydrate-containing foods may be added and the carbohydrate tolerance of the patient be determined. In those cases able to utilize a considerable amount of starch, the accessory diet may be varied from day to day, and use may be made of the following table, which gives the carbohydrate equivalent of one slice (1 ounce or 30 grams) of white bread, containing approximately 15 grams of starch.

Foods.	Household Measure.	Gm.
Uncooked Flours, etc.:		
Barley	1 h. tbsp.	21
Buckwheat	1 "	19
Cornmeal	1 "	20
Farina	1 "	20
Hominy	1 "	18
Macaroni	1 "	20
Noodles	1½ "	20
Oatmeal	1 "	22
Rice	1 "	18
Rye flour	1 "	18
Spaghetti	1½ "	20
Vermicelli	1½ "	21
Wheat flour	1 "	20
Bread and Crackers:		
Bread	1 slice.	30
Breakfast biscuit (Huntley & Palmer)	3	18
Cornbread	1 slice.	32
Roll (Vienna)	½	25
Uneeda Biscuit	3	18
Zwieback	1⅓	20
Cooked Cereals:		
"Force"	5 h. tbsp.	18
Farina	2½ "	125
Grapenuts	1½ "	20
Hominy	1½ "	90
Macaroni	2 "	100
Oatmeal	2½ "	130
Rice	½ "	60
Shredded wheat biscuit	¾	22

Foods.	Household Measure.	Gm.
Cooked Vegetables:		
Artichokes	1 medium.	320
Beans (baked—canned)	2 h. tbsp.	75
Beans, lima	1¼ "	50
Beets	6 "	200
Carrots	13 "	440
Okra	4 "	200
Onions	3	300
Parsnips	4 slices.	120
Peas, green	3 h. tbsp.	100
Potato (baked)	½ medium.	60
Potato (boiled)	½ "	70
Potato (mashed)	1½ h. tbsp.	80
Potato, sweet (boiled)	⅓ medium.	35
Squash	2 h. tbsp.	100
Turnips	3 "	210
Fruits:		
Apple	1 medium.	120
Apricots	2 large.	120
Banana (without skin)	½ medium.	75
Cherries	....	90
Currants	5 h. tbsp.	120
Grapefruit	½ small.	150
Huckleberries	3½ h. tbsp.	90
Lemons	2 medium.	210
Muskmelon	⅓	300
Nectarine	1	100
Olives, green	20	180
Orange	½ large.	150

Foods.	Household Measure.	Gm.
Fruits:		
Peaches	1½ medium.	150
Pear	1 small.	100
Pineapple	3 slices.	150
Plums	2 medium.	75
Raspberries	4½ h. tbsp.	120
Strawberries	8 "	200
Watermelon	Large slice.	300
Dried Fruits:		
Apples	3 small.	22
Apricots	3 large.	24
Currants	1½ tbsp.	20
Dates	3	19
Figs	1 large.	12
Prunes	2 "	24
Raisins	10 "	23

Foods.	Household Measure.	Gm.
Milk and Cream:		C.c.
Buttermilk	1½ tumbler.	300
Cream, 16 per cent.	1½ "	300
Cream, 40 per cent.	1½ "	300
Koumiss	1½ "	300
Whole milk	1½ "	300
Nuts:		Gm.
Almonds	60	90
Brazil	30	180
Chestnuts (roasted)	15	40
Cocoanut	1 slice (3 x 2 in.)	50
Filberts	100	100
Peanuts	40	80
Pecans	35	110
Pistachio	190	95
Walnuts	30	125

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ACROMEGALY

History and Physical Examination of a Case of Acromegaly, Illustrating the Chief Features of the Disease. Possible Association of a Myxedematous Factor.

Classification of the Endocrine Glands from an Embryologic Standpoint. The Interrelationship of the Ductless Glands. The "Accelerator" and "Inhibitory" Action of the Hormones of the Endocrine Glands. The Anatomy and Histology of the Anterior and Posterior Lobes and of the Pars Intermedia of the Pituitary Gland. The Functions of the Two Lobes of the Pituitary.

Lesions of the Pituitary Found in Acromegaly. Classifications of States of Dyspituitarism. Treatment of Acromegaly.

THE case I desire to present to you today is one that illustrates a very interesting condition dependent upon a disturbance of the functions of one of the ductless or endocrine glands. Our knowledge of the various affections resulting from diseases of these glands has been materially added to in the past decade and a half, and the interest in the subject has been quite recently manifested by the appearance in this country early this year of the first number of a special Journal devoted exclusively to this subject and called "Endocrinology." Many of the symptom-complexes due to disorders of these glands had for a long time remained clinical enigmas, but, with out increasing knowledge of the subject, these patients now rank among the most interesting cases met with in clinical work.

The patient, A. S., is a woman sixty-seven years of age and came under my personal observation in December, 1915, although

she was first admitted to the Medical Department of the Outpatient Clinic in October, 1910, at which time she was complaining of severe headache, a feeling of weight over the chest, slight cough, and obstinate constipation.

She has had no serious infections. Her catamenia began at thirteen. She has borne two children and had two miscarriages. The patient had become prematurely amenorrheic, as is so often the case in the disease under consideration. An important point in the history obtained at the first visit was that even at that time she had suffered from severe headaches for many years.

The recorded physical examination at this visit revealed nothing of importance, and there is no record of her then presenting any of the facial or other features she now exhibits, although it is quite probable that they existed in a minor degree. The records show that she was given dietetic and other directions for her constipation. She did not return until October 22, 1912, at which time she was complaining of headache and general weakness. There was again an interruption in her visits until November 15, 1915, when she complained of pain in the right lumbar region and a peculiar feeling in her chest, which, in the light of the subsequent diagnosis, may have been due to nerve-root disturbances connected with the vertebral changes in this disease.

She did not return until December 15, 1915, when she came under the observation of Dr. H. R. Carter, who first recognized the fact that the patient presented undoubted signs of acr megaly. It was at this time that I first saw her and concurred in the diagnosis. At this visit it was noted that she had a rather coarse tremor of the right hand which resembled rather closely that seen in paralysis agitans. From that date up to the present time she has paid occasional visits to the Dispensary. On all occasions she complained of intense headaches. In order to insure her being here today we had to send a conveyance for her, because she said that her headaches were sometimes so severe that she could never tell when she would feel well enough to leave her house. Frontal headache has been her chief subjective symptom throughout.

Physical Examination.—On observing the patient you will at once be struck with the rather massive character of her features. The nose is decidedly large and broader than normal. The malar bones and supra-orbital ridges are prominent. You will observe the massive character of the lower jaw and its striking forward projection (prognathism). When we ask her to close her jaws tightly together you will notice that the teeth of the lower jaw project considerably beyond those of the upper, the reverse of what happens in normal individuals. We find that the teeth are rather widely separated. The wrinkles over the forehead and the nasolabial folds are much deeper than normal, showing the changes that have taken place in the subcutaneous tissue.

The examination of the chest shows some striking features. You will observe that there is a marked dorsal bowing of the spine. This increases the anteroposterior diameter, giving a conformation similar to that seen in emphysema.

The hands are characteristic. The fingers are rather short, stubby, and broad, producing the so-called spade-like hand. The finger-nails are broad and short and do not show the normal transverse and vertical curving. All of the tissues of the hand are hypertrophied and the lines of the palms are much deepened. You will observe that there is a slow coarse tremor of the right arm and hand without any Parkinsonian facies.

The feet are much enlarged and show the general characteristics manifested by the hands.

The skin over the whole body is rather dry and harsh and there is a little bagginess of the skin over the backs of the hands, which at least suggests a possible associated myxedematous factor in the case. There is slight increase of the adipose tissue of the whole body. There is no special increase in the development of hair (hypertrichosis) in this case.

In searching for possible "neighborhood" or "regional" symptoms in this case the most striking one is her intense frontal headache, which no doubt is due to pressure of the diseased pituitary or surrounding structures. The eyes often manifest neighborhood signs in these patients. On rough testing we find that

she has marked restriction of her temporal fields of vision suggesting strongly a bitemporal hemianopsia, but accurate perimetric measurements have not been taken. The optic disks show some signs of atrophy. These are the only positive signs in this case. Some acromegalics show evidences of pressure on the third nerve and on the abducens. These signs may be unilateral. Occasionally exophthalmos occurs. Epistaxis and rhinorrhea have been noted. Somnolence, irritability, depression of spirits, and general change in temperament occasionally occur.

It is interesting to note the changes in the cardiovascular system. There is definite sclerosis of the radials and brachials and the systolic blood-pressure is increased to 185. There is moderate left-sided cardiac hypertrophy, with an accentuated aortic second sound. This arteriosclerosis has been found to be a fairly constant feature in acromegaly by Russell and others.

The urine has shown faint traces of albumin. Dr. Towles has kindly tested her carbohydrate tolerance by giving 200 grams of glucose on an empty stomach and has tested the five subsequent voidings for glucose. In the third specimen there was a suspicious reduction of Fehling's solution. In none of the specimens, however, did the fermentation test prove positive at the end of twenty-four hours. We can, therefore, reasonably conclude that the patient has an increased carbohydrate tolerance.

Roentgenographic Examination.—On December 9, 1915, Dr. F. H. Baetjer took roentgenograms of the skull and hands. These I am now able to show you. Dr. Baetjer's report is as follows: "Large sella. Thickened skull. Phalanges much thicker than normal. Marked tufting of the terminal phalanges. The whole picture suggests acromegaly."

Roentgenograms of the skeletal bones have not been taken, but I am able to demonstrate to you very well the bony changes which occur in this disease on this skeleton obtained at autopsy a number of years ago on a former patient in the medical wards. This case has been reported in the literature by Dr. Thayer. You will observe the deep broad sella turcica; the massive lower jaw; the enlarged malar and nasal bones and zygomata; the

exaggerated frontal and supra-orbital ridges; the wide separation of the teeth; the dorsal bowing of the spine and the lipping and exostoses of the individual vertebræ; the exaggeration of the normal ridges on the long bones, especially at the points of muscle and tendinous attachments; the broadened phalanges, and the fan-shaped appearance of the terminal phalanges of the fingers and toes.

Diagnosis.—With this review of the physical findings in this case we are justified in making a definite diagnosis of acromegaly. The dryness of the skin and slightly baggy condition of the skin over the backs of the hands suggests the possibility of an associated myxedematous factor due to insufficiency of the thyroid secretion. The coarse tremor of the right arm and hand points strongly to the early phases of paralysis agitans, although this could be a senile tremor.

Our knowledge of acromegaly dates from 1886, when Pierre Marie described 2 cases of his own and others in the literature distinguishing it from other affections with similar symptoms. In 1889 he drew attention to the relationship between affections of the pituitary gland and acromegaly and gigantism. Since Marie's report an extensive literature on diseases of the pituitary gland has grown up. The best available consideration of the whole subject is this excellent volume by Cushing entitled "The Pituitary Body and its Disorders."

The presentation of this case affords us an opportunity to review some facts concerning the anatomy and functions of the pituitary gland, which, as you know, is situated in the sella turcica at the base of the skull. As the pituitary is one of the endocrine or ductless glands it might be of interest, at this point, to give D. Noël Paton's classification of the various endocrine glands from an embryologic standpoint.

Embryologic Classification of the Endocrine Glands.

I. From the Nervous System.
   (1) The Chromaffin Tissue, exclusive of the Adrenals.
   (2) The Hypophysis Cerebri—the Pars Nervosa of the Posterior Lobe.

II. From the Buccal Cavity.
  (1) The Thyroid.
  (2) The Pituitary—The Anterior Lobe and Pars Intermedia.
III. From the Intestine.
  (1) The Pancreas.
  (2) Mucosa of the Small Intestine.
IV. From the Branchial Arches.
  (1) The Parathyroids.
  (2) The Thymus.
V. From the Mesothelium of the Genital Ridge.
  (1) The Gonads—Testicles and Ovaries.
  (2) The Interrenal Bodies—The Adrenals.

The Interrelationship of the Ductless Glands.—In considering a disease dependent upon the disturbance of function of any one of the ductless glands, the possible interrelationship of the function of this gland and that of the others has constantly to be kept in mind, for in many instances the symptom-complex is a polyglandular manifestation. All the endocrine glands produce an internal secretion or "hormone." These hormones possess in many instances either an "accelerator" or "inhibitory" influence upon the hormone of one or more of the other endocrine glands and upon metabolism.

To the accelerator group belong the hormones of the thyroid, adrenals, and hypophysis.

(1) All three increase protein exchange.

(2) The adrenals cause mobilization of carbohydrates.

(3) The thyroid causes increased fat destruction.

To the inhibitory group belong the hormones of the pancreas and parathyroids.

(1) Both retard protein exchange.

(2) Both retard carbohydrate exchange, the hormone of the pancreas being the more active of the two.

(3) The pancreas causes a decrease of fat destruction.

The Anatomy of the Pituitary Gland.—A brief account of

the anatomy of the gland may be of interest. Following the description of Herring, we speak of three divisions:

(1) The Anterior Lobe, or Pars Anterior.

(2) The Posterior Lobe, or Pars Nervosa.

(3) The Pars Intermedia—the modified cellular structure derived from the anterior lobe, which surrounds the posterior lobe and extends upward along the stalk of the infundibulum.

The anterior lobe is derived from the pharyngeal pouch described by Rathke in 1838, and is completely of ectodermic origin. It resembles somewhat the thyroid in structure. It is extremely vascular, the blood-supply being derived most probably from branches of the carotids. The cells of the anterior lobe are classified according to their staining affinity. Some are chromophile (either eosinophilic or basophilic) and the remainder are chromophobe.

"In the pars intermedia, investing the posterior lobe, the cells are of a different type and without eosinophilic granules, and it is here that one finds a tubular or acinar distribution of cells which have a tendency to secrete colloid, resembling in appearance the secretion characteristic of the thyroid gland. These cells are seen, under certain circumstances, actually to invade the pars nervosa, into which the product of their secretion is directly discharged, whence, as Herring first pointed out, it seems to pass through tissue channels toward the infundibular cavity, to find its way ultimately between the ependymal cells into the cerebrospinal cavity of the third ventricle" (Cushing).

The pars nervosa is composed of neuroglia and ependymal tissue, and serves probably to transmit the secretion of the pars intermedia and perhaps of the anterior lobe.

The total weight of the normal gland is approximately 0.6 gram.

The Functions of the Pituitary Gland.—As a result of the researches of many investigators we now know that the gland is essential to life. Cushing and his associates demonstrated that complete hypophysectomy resulted in the death of the animal. While our knowledge as to the functions of the pituitary gland may not yet be complete, it may prove instructive to

enumerate the various functions which the two lobes are believed to possess.

Functions of the Anterior Lobe.—(1) It influences skeletal growth. If a hypersecretion (hyperpituitarism) occurs during the years of the individual's growth and before the ossification of the epiphyses, gigantism occurs—the Launois type. If the hyperactivity occurs after the individual's growth has been attained, then acromegaly results. It is interesting to note that the changes in the facial appearance and the increased size of the hands and feet during pregnancy are believed to be due to a temporary increased activity of the anterior lobe. If a diminished secretion (hypopituitarism) occurs in childhood a form of infantilism develops, to which attention was first called by Fröhlich. This condition is known as Fröhlich's syndrome, or dystrophia adiposogenitalis. It is characterized by small stature, amenorrhea in females, infantile genitalia in both sexes, hypotrichosis, excessive deposition of fat, and increased carbohydrate tolerance. When the hypopituitarism occurs in adults, adiposity and sexual infantilism of the reversive type develop.

(2) Injections of the extract of the anterior lobe causes an increase in temperature.

(3) The hormone of the anterior lobe accelerates thyroid function.

(4) As noted above, it powerfully increases sexual development and growth of the hair.

Functions of the Posterior Lobe.—(1) The extract causes a striking increase in the blood-pressure, as Schaefer and Oliver and Howell have shown.

(2) It is a powerful diuretic. I wish to call your attention at this point to the modern conception as to the causes of a large percentage of the cases of symptomatic diabetes insipidus. It has now been shown that these cases are due to diseases of the pituitary gland probably involving the pars intermedia of the posterior lobe. Injections of pituitrin have yielded most gratifying results on the symptoms of this distressing disease.

(3) It has a powerful influence over carbohydrate metabolism.

In hyperpituitarism, such as one sees in the early stages of acromegaly, there is found to be a diminished carbohydrate tolerance and there may even be a spontaneous glycosuria. This is due to the stimulating effect that tumors of the anterior lobe have on the hormone of the posterior lobe. In the later stages of acromegaly, however, when a certain amount of adiposity develops due to an associated hypopituitarism, there is always an increased carbohydrate tolerance. In the hypopituitarism of dystrophia adiposogenitalis the carbohydrate tolerance is increased two-, three-, or fourfold. Cushing and his associates, in experimenting on animals, have shown that removal of the posterior lobe of the hypophysis leads to obesity of the animal and a very striking increase in the carbohydrate tolerance. Out of 176 cases of acromegaly reported in the literature up to 1908, Borchardt found that spontaneous glycosuria occured in 35.5 per cent. of the cases. Cushing comments on the discordant results that different observers have found in the study of the carbohydrate tolerance in acromegaly. Some have found an actual glycosuria, others only a diminished tolerance, and still others a decidedly increased tolerance. He is of the opinion that these discrepancies are entirely dependent on the stage of the disease in which the case comes under observation. He holds that the adenomas or other tumors of the anterior lobe, which cause the characteristic features of acromegaly, also produce hyperplasia and overactivity of the posterior lobe in the early stages (hyperpituitarism) with the result that an excess of the secretion of the posterior lobe (pars intermedia) reaches the circulation and a lowered tolerance to carbohydrates ensues. In the later stages a hypoplasia of the pars intermedia of the posterior lobe occurs (hypopituitarism), with the result that there is an increased tolerance to carbohydrates, which no doubt accounts for the tendency to moderate obesity in acromegalics. In the pituitary glycosurias the blood shows a hyperglycemia. This hyperglycemia is probably due to the fact that the oversecretion of the posterior lobe causes an increased mobilization of the stored glycogen of the liver. The glycosurias of pregnancy may possibly also be explained in the same way.

(4) Rinon and Delille believe that the posterior lobe extract accelerates the adrenal and inhibits the thyroid function.

(5) Ott, Schaefer, and MacKenzie have shown that the extract is even a more powerful galactogogue than the extract of the corpus luteum.

(6) The extract has a powerful influence in exciting unstriped muscle to contract. This knowledge has led to the extensive use of pituitrin to facilitate uterine contractions during parturition and also to stimulate intestinal peristalsis in marked meteorism, such as one sees in severe pneumonias and other infections.

Lesions of the Pituitary Found in Acromegaly.—Practically all cases of acromegaly show changes in the pituitary gland. The commonest lesions found are hyperplasia, adenoma, fibroma, or sarcoma. Not infrequently cysts are found, but these probably result in most cases from degenerative changes in pre-existing tumors. The symptoms of the disease are dependent in part upon the disturbance of the functions of the gland resulting from the tumor growth, and in part upon the pressure effects exerted by the tumor on adjacent structures—the so-called "neighborhood" or "regional" symptoms.

Classification of States of Dyspituitarism.—We have already referred to the fact that symptoms which are dependent upon overactivity of the pituitary gland are spoken of as "hyperpituitarism," and that those due to lessened functional activity of the gland are referred to as "hypopituitarism." In many cases of acromegaly, particularly those of long standing, however, we we have a symptom-complex in which there are evidences of both states existing in the same case. Thus we often see the characteristic skeletal changes dependent upon overactivity of the anterior lobe, in association with increased thickness of the subcutaneous tissue, amenorrhea, and increased carbohydrate tolerance, resulting from hypo-activity of the posterior lobe. Cushing refers to these cases as instances of disturbed function of the pituitary and has applied to them the name "dyspituitarism."

It has been found that the cases of dyspituitarism present a rather varied symptom-complex, depending upon whether the

glandular or neighborhood symptoms predominate, and whether there are polyglandular manifestations, etc. Cushing, in analyzing his cases, divided them into five separate groups:

Group I.—Cases of dyspituitarism in which not only the signs indicating distortion of neighboring structures but also the symptoms betraying the effects of altered glandular activity are outspoken.

Group II.—Cases in which the neighborhood manifestations are pronounced, but the glandular symptoms are absent or inconspicuous.

Group III.—Cases in which neighborhood manifestations are absent or inconspicuous, though glandular symptoms are pronounced and unmistakable.

Group IV.—Cases in which obvious distant cerebral lesions are accompanied by symptomatic indications of secondary pituitary involvement.

Group V.—Cases with a polyglandular syndrome in which the functional disturbances on the part of the hypophysis are merely one, and not a predominant feature of a general involvement of the ductless glands.

Treatment of Acromegaly.—Up to a decade and a half ago the treatment was very unsatisfactory and purely symptomatic. The efforts to relieve the severe headaches occurring in some of the cases were often ineffectual, even with large doses of morphin.

In recent years surgical treatment has done much for these unfortunate victims, who often suffer from intense headaches and other neighborhood symptoms. The object sought is the removal of the diseased gland or of any neighboring tumor pressing upon the gland. The ability to successfully approach the pituitary by one or other of the various routes constitutes one of the most important surgical triumphs of recent years. A successful hypophysectomy often completely relieves these victims of their excruciating headache, stops the progress of the disease, and saves lives which would otherwise be lost as a result of the progressive development of pressure-symptoms.

It will be natural for you to inquire whether organotherapy has been of benefit in these cases. I am glad to be able to inform

you that it has been materially helpful. It should always be instituted after hypophysectomy, since life is not compatible with complete removal of the gland and its administration combats the somnolence and tendency to adiposity, which develops owing to the increased carbohydrate tolerance. In the early days of pituitary organotherapy extracts of the whole gland were used. As might be expected, it has been found that the symptoms in cases of acromegaly still manifesting hyperpituitarism features have sometimes been made worse by administration of extracts of the whole gland. The cases most benefited are those in which the anterior lobe manifestations have become quiescent and in which hypopituitarism features, due to hypo-activity of the posterior lobe, dominate the picture, such as subnormal temperature, amenorrhea, increased carbohydrate tolerance, and progressive adiposity. You will fully appreciate that extract of the posterior lobe would be indicated under these circumstances, and this preparation is now available.

The dosage of the posterior lobe extract has to be worked out for each individual case. This dosage is ascertained by studying the effect it has on the patient's carbohydrate tolerance. The procedure can probably be best understood by the following quotation from Cushing: "Comment has been made on the fact that in experimental as well as in clinical conditions of hypopituitarism associated with a high sugar tolerance, the assimilation limit can be lowered by the coincident administration of glandular extracts, particularly of those obtained from the posterior lobe. Thus in hypopituitarism the rational dosage of glandular extract to be administered by mouth can possibly be determined by giving the individual daily an amount of glucose or levulose sufficient to produce a temporary mellituria in a normal individual of equal body weight; meanwhile an increasing amount of the extract is administered daily until, under the conditions of increased carbohydrate tolerance which the patient exhibits, hyperglycemia occurs with a trace of sugar in the urine."

The extract may be administered by mouth. After its administration there is not infrequently a lessening in the degree of adiposity and an improvement in the mental alertness. The

most striking benefit, however, is obtained in the typical cases of hypopituitarism, such as one sees in Fröhlich's syndrome, the dystrophia adiposogenitalis. Sometimes oral administration of the extract does not yield very satisfactory results. In these cases recourse may be had to hypodermic administration of the extract. Goetsch, in his studies of experimental canine hypopituitarism, found that the subcutaneous administration of posterior lobe extract was more effective in lowering the assimilation limit for sugars than the administration by mouth in the proportion of 4 to 1, and that in about a ratio of 2 to 1 the intravenous administration was more effective than the injection of the extract into the subcutaneous tissues.

COMBINED SCLERODERMA, RAYNAUD'S DISEASE, AND CHRONIC ARTHRITIS

History and Physical Examination of the Case Presented.

Brief Discussion of the Main Features of Scleroderma. Histologic Examination of the Skin. Possibility that the Disease is Due to a Disturbance of the Function of One or More of the Endocrine Glands. Types of the Disease Met With. The Treatment of the Affection.

The Four Stages of the Circulatory Disburbances in Raynaud's Disease. The Complications Met With. Differential Diagnosis from Vascular Affections Simulating it. The Treatment of the Disease.

The Relative Frequency of Scleroderma and Raynaud's Disease in Association with Arthritis.

One of the cases I desire to present before you today exhibits an interesting and rather unusual group of symptoms.

The patient, A. H., is a married woman aged thirty-five. The family history is unimportant. There is no history of other members being similarly affected. She had the usual diseases of childhood. The menstrual functions have been normal and she has had two children. In 1913 she was vaccinated and was very ill afterward, having been confined to bed for four weeks. Soon after this she began to complain of numbness and coldness in the hands and feet and of pains in the ankles on walking. She states that if her hands become cold or if they are immersed in water for any length of time, one or more fingers become perfectly blanched and feel numb. In the course of about one hour the same fingers become a deep bluish-red color. On two or three occasions blebs have developed on the pads of the distal phalanges and later the skin over these areas has become black and very hard. Eventually she cuts the black, hard skin off, as these areas are painful when she strikes them against firm objects. She has the same blanching, numbness, and subsequent

blueness of several toes of both feet. There has been no severe pain in the digits in any of the attacks. The ears and nose have never been involved.

Three years ago the patient had a severe attack of tonsillitis and since then she has had a good deal of soreness and stiffness of the right wrist and of the joints of the hands and insteps. In the last few months she has observed that the skin over the fingers has become somewhat shiny and thickened, and she has found that it has been increasingly difficult to flex the fingers into the palms of the hands.

Eighteen months ago she began to have successive attacks of a skin eruption which she described as hives and which was very itchy. More recently the eruption has become papular and there have also been some small pustules.

The patient first sought hospital advice in the Dermatological Department of the Dispensary on August 28, 1916, at which time a diagnosis of urticaria was made. On September 19, 1916. she was referred to the Medical Out-patient Department. She has since been treated in the Throat Department for Chronic Tonsillitis; in the Surgical Department for Ingrowing Toe-nails; in the Orthopedic Department for Chronic Infectious Arthritis, having received numerous bakings of the affected joints; and in the Dental Department for pyorrhea and carious teeth.

Physical Examination.—The patient is sparely nourished, her present weight being 115 pounds. Three years ago she weighed 159 pounds. You will, I think, be at once struck with her facial appearance. There is distinct shortening of the upper lip, which is thinner than usual. The skin over it is glossy, and distinctly thicker and firmer than normal. That over the malar bones and over the forehead is smooth, slightly shiny, and a trifle thickened. The facial lines are obliterated, giving the face a somewhat expressionless appearance. The most striking changes have taken place in the skin over the fingers of both hands. The fingers are somewhat enlarged. The skin is glossy, thickened, firm, and cannot be picked up between one's fingers, and the transverse lines are obliterated. The tightness of the skin prevents her from "making a fist." Nowhere else on the body do we

find similar skin changes. I wish to draw your attention to the striking patches of bronzed pigmentation over the backs of the hands, a feature not infrequently associated with the skin changes we have already described.

I desire to point out now that an entirely different group of skin changes coexist in this case. Just before the patient came into the clinic she was asked to immerse her right hand in a basin of cold water. You will see that the skin over the last two phalanges of this hand is of an almost marble-white color and the patient says that these fingers are distinctly numb. There is no striking cyanosis of any of the fingers or toes, but they are all rather cold. Over the tips of the index and middle fingers of the right hand there are areas about 0.5 cm. in diameter where the skin is black and hard. Several of these small areas of gangrenous skin have developed in the past.

You will also note that over the face and trunk she has numerous acne-like papules. At the present time there are no urticarial wheals.

As noted in the history, the patient has had for three years arthralgic pains in numerous joints. While there is no striking deformity of the joints, her right wrist is somewhat stiff, and Dr. F. H. Baetjer's roentgenographic examination of this region reveals evidence of "an infectious arthritis at the end of the right radius." The interdigital joints of the fingers of both hands are slightly thickened and stiffened, and these joint changes may in part contribute to her inability to completely flex her fingers. Walking at times causes pain in the insteps, and examination shows some discomfort on manipulation of the tarsal joints.

The examination of the throat shows that the tonsils are not appreciably enlarged, but are cryptic and adherent. Her paranasal sinuses have been transilluminated and reveal no evidences of infection.

The investigation of the teeth shows a slight pyorrhea which is being treated, and some decayed roots have already been extracted.

The radial and brachial arteries show only slight sclerosis. The dorsalis pedis arteries pulsate normally. The heart is nor-

mal. The thyroid shows no recognizable changes, but at times she has had tachycardia. The urine and blood Wassermann are both negative.

Diagnosis.—From a consideration of the history and physical findings in this case we are justified in making a diagnosis of scleroderma, Raynaud's disease, and chronic infectious arthritis. The teeth, tonsils, or the vaccination infection are the most likely primary sources of infection causing the latter.

It may be of interest to review some of the salient features of scleroderma and of Raynaud's disease.

Scleroderma.—It is believed to be a nutritional disturbance of the skin, patchy or diffuse, leading to induration and atrophy.

Although it is a rare affection, it is probably more common in this country than the statistics would indicate. From the opening of the Johns Hopkins Hospital in May, 1889, to May, 1905, 18 cases came under the observation of Sir William Osler, who was much interested in the disease.

Women are more frequently affected than men, the statistics of Lewin and Heller showing 67 per cent. in the former. The majority of the cases occur between twenty and forty years of age. In a few instances heredity seems to have been a factor. Acute infections are believed to play an important part in many instances. Cases have been reported following the acute specific fevers. It is of interest to note that in the case before you the symptoms seem to have followed a severe infection following vaccination. Many cases have followed in the course of an infectious arthritis. An arthritis exists in our patient.

Histologic examination of the skin generally shows sclerosis of the smaller arteries, which may manifest endarteritic changes and sometimes obliteration of the lumen. There is an increase of the elastic fibers below the papillary layer, extending into the subcutaneous tissue. No constant lesions are found in the central or peripheral nervous systems.

No definite clew has been found to explain the true nature of the disease. Osler says: "The analogy of myxedema, to which scleroderma is the cutaneous antithesis, suggests that it may be caused by some alteration in an internal secretion, or some dis-

turbance of that nice balance between the various internal secretions, and which plays such an important rôle in nutrition. The disturbances of pigmentation, as intense as any which we see, may depend on some adrenal insufficiency. The frequency with which the acute forms follow an infection is paralleled by the thyroid insufficiency and atrophy caused by myxedema after a fever such as measles and scarlet fever."

Another view held is that scleroderma is due to a terminal endarteritis. Lewin and Heller and others regard the disease as an angiotrophic neurosis depending upon unknown changes in the trophic center.

There are three modes of onset—the simple atrophic, the edematous, and the erythematous. The first is the commonest. Rarely, localized areas of edema with depressions between are manifest at the onset. The erythematous onset may be of two types: in one a diffuse erythema and swelling occur in the face or on parts of the trunk; in the other the picture is that of the vasomotor disturbances of the hands and feet similar to that seen in Raynaud's disease. The possibility of this case being of this type has to be considered, but the existence of marked local syncope and of actual gangrenous areas on the tips of the fingers leaves little doubt that she is suffering from true Raynaud's disease.

As to distribution, the face and extremities are most commonly involved. In rare instances the condition may be universal.

Two groups of cases occur so far as the extent of the disease is concerned—the circumscribed and the diffuse forms.

In the circumscribed there are patches ranging from a few centimeters in diameter to the size of the hand or larger. These areas occur most commonly over the breasts in women and about the neck. There may be deepening in the skin pigmentation, actual leukoderma, or a combination of both over the affected areas.

Although less common, the diffuse form is much more serious. It generally develops first in the extremities or on the face. As to localization, Lewin and Heller's statistics showed that in 66 cases it was universal; in 203, regions of the trunk were

affected; in 193, parts of the head and face; in 287, portions of one or other of the upper extremities; and in 122, portions of the lower extremities. When the extremities are involved the skin of the whole member may be affected and function be materially interfered with. In the universal type the unfortunate individual may become perfectly helpless.

Trophic changes may occur. Onychia has been present. The hair may fall out over the affected area or atrophy of the pigment of the hair over the area may occur. The muscles of the affected part may be fibroid and atrophic. Even the bones of the involved member may be atrophic.

Raynaud's disease may be associated in some of the cases. One must always keep in mind, however, that this may merely be an end-stage of the so-called erythematous type of scleroderma. In many of the cases an arthritis antedates the onset of the skin manifestations.

There are acute and chronic forms. The former generally occur in children and follow acute infections. Its development in these cases may be very rapid. Usually the disease is very chronic. Many cases have lasted fifteen years or longer. The patients are likely to succumb to pulmonary tuberculosis or nephritis. Occasionally spontaneous arrest of the disease occurs.

The treatment is very unsatisfactory. Warm baths and massage should be given a thorough trial. Electricity may be used. Of all the numerous medicinal agents that have been advised, the thyroid preparations have had the widest vogue. They should be thoroughly tried out. Some cases have possibly been helped. We started this patient on 2-grain doses of desiccated sheep's thyroid three times daily, but before a week elapsed she developed symptoms of thyroidism, characterized by marked nervousness, sleeplessness, tachycardia, and great irritability of the skin, and the drug was temporarily discontinued. Fibrolysin has been useless. Osler says: "I doubt if any remedy has an influence on the disease unless it be the *x*-rays, which should be given a thorough trial."

Raynaud's Disease.—This disease has received its name from Maurice Raynaud, a Frenchman, who first described it in a

Thesis published in 1862, and who made subsequent contributions to the subject in 1872 and 1874.

It is a vascular disorder, without organic change in the vessels, chiefly observed in the extremities, in which a persistent ischemia or a passive hyperemia leads to a disturbance of function or to a loss of vitality with gangrene.

In its characteristic form the circulatory disturbance manifests itself in four stages: (1) Local syncope. (2) Local cyanosis or asphyxia. (3) Active hyperemia. (4) Necrosis or gangrene.

The local syncope, the first stage, is the most characteristic symptom. The fingers are most often affected, then the toes, the ears, and the tip of the nose. A dead white anemia develops, and the affected area is cold and clammy. The patient may complain of numbness or a sensation of pins and needles in the involved part. Actual pain is rare at this stage.

In the second stage, of local cyanosis or asphyxia, the color varies from a reddish blue to a blue black. The return of blood to the affected part is probably due to a back-flow through the capillaries from the veins, as in frost-bite. The part still remains very cold. The color is due to the fact that the circulation is so slow that the capillaries are filled with red corpuscles, the hemoglobin of which is deoxidized. It is in this stage that the severe pain usually begins.

The third stage of active hyperemia may directly follow the syncope, but it usually follows the asphyxia. After the cyanosis has lasted from several hours to a day or more, the color begins to change, the patient feels a throbbing in the affected part, the radial pulse gradually becomes full and large, a capillary pulse may be seen in the nails, and the cyanosis is replaced by a bright pink. Sometimes all these three stages may be seen together in different fingers of the same hand.

If the asphyxia persists and the circulation is not re-established there is danger of the final stage, that of necrosis or gangrene, developing. This may follow either the stage of syncope or cyanosis, but more frequently the latter. The skin gradually becomes black. Blebs may form and break. The skin then becomes dry and the separation of the dead skin usually is slow

and painful. Sometimes the necrosis is superficial. On the other hand, it may be deep, involving the bone and the separation of the affected part may have to be assisted by surgery. The gangrene is often but not always symmetric.

The disease is comparatively rare. Women are more frequently affected than men. Monro's series showed 62.5 per cent. in the former and 37.5 per cent. in the latter. It occurs at all ages, but 60 per cent. occur in the second and third decades. There have been instances in which several members of a family have been affected. Neurotic and hysteric patients are especially prone. Damp and cold weather predispose to attacks. The patients are always freer in warm weather. In 43 per cent. of Monro's cases one or both of the upper extremities were involved. The nose, chin, ears, nates, and eyelids may be attacked.

The disease manifests itself in varying degrees of severity. We speak of mild (formes frustes), moderate, and severe types. In the severe forms with intense pain it is really a terrible malady.

The nature of the disease is as yet not definitely determined, but it is believed to be due to some factor which causes angiospasm of the peripheral vessels.

Various complications may occur. If we accept the angiospasm theory, it is quite natural that we might expect ocular and cerebral complications due to spasm of the retinal and cerebral vessels. These complications actually occur. Temporary amblyopia due to spasm of the retinal vessels, and transient aphasia and transient hemiplegia due to spasm of the cerebral vessels have occurred. H. M. Thomas has reported a case in which epileptiform seizures developed during the attacks of local cyanosis.

Albuminuria may occur during the attacks and numerous cases have occurred in which hemoglobinuria developed.

Scleroderma and arthritis have been reported in a number of instances, and this association exists in the patient before you.

The diagnosis is usually not difficult. Other conditions may simulate it. In the acute specific fevers, particularly in typhus and malaria, areas of multiple gangrene may occur.

A few years ago we had in the Medical Wards a case of symmetric gangrene over the buttocks complicating malaria. The difference in distribution and the history usually renders the diagnosis in these cases easy. The senile gangrene of arteriosclerotics and the gangrene of diabetics due to an obliterative endarteritis of the peripheral vessels should give no diagnostic difficulty. The customary obliteration of the pulse in the affected extremity is diagnostic. The pain, cyanosis, and gangrene in the thrombo-angiitis obliterans of Buerger resemble Raynaud's disease in the earlier stages, but its restriction almost entirely to young male Russian Jews, together with the obliteration of the pulse in the peripheral vessels, is diagnostic. In this condition there is a primary thrombosis in both the arteries and veins, with subsequent changes in the vascular walls. The local syncope phase, so characteristic of nearly all cases of Raynaud's disease, is lacking in nearly all these conditions. Local asphyxia has been noted in diabetic gangrene, however. The trophic disturbances and pains of syringomyelia closely simulate Raynaud's disease, but the associated disturbances of sensation and motion in the former render the diagnosis easy.

The treatment is not very effective, yet considerable can be done for the milder cases. Warmth is a very essential factor, and when the finances will permit it the patient should be advised to seek a warm climate during the winter months. Where this is not possible, the extremities should be kept as warm as possible. Massage, electricity, and hydrotherapy are also helpful in these cases. Massage thoroughly carried out in the cases which have not reached the necrosis stage is most helpful. Galvanism, as directed by Barlow, sometimes gives relief. The affected extremity is immersed in a salt bath. One pole is placed in contact with the upper part of the limb above the level of the water and the other is placed in the water, thus converting the water and salt into an electrode. The current is intermittently broken so as to cause mild muscular contractions in order to help re-establish the circulation. Radiant heat baths are sometimes comforting.

In the severe forms three indications have to be met: (1) To

relieve the pain. Radiant heat may be helpful. Local sedative applications may be tried, such as compresses saturated with hot lead-and-opium lotion. Morphin may be necessary, but should be used as a last resort. (2) To re-establish the circulation in the asphyxiated area so as to prevent necrosis if possible. Hot douches, immersing the extremity in hot water, the hot-air bath, or radiant heat should be used. Cushing found the repeated use of Esmarch's bandage, in order to secure active hyperemia, helpful. The extremity is bandaged lightly and rendered anemic and then the tourniquet is applied for a few minutes. At first the pain may be increased. On removal of the tourniquet an active hyperemia occurs, often with considerable relief to the pain and with more favorable conditions of nutrition established. (3) Local treatment of the gangrenous part. Antiseptic poultices may favor the separation of the gangrenous area, always at best a slow procedure. Putting the patient in a continuous warm bath for two or three weeks, especially if there is great pain, may be tried. Surgical intervention in some cases may be advisable.

The medicinal treatment is unsatisfactory. Amyl nitrite inhalations or nitroglycerin by mouth may be tried. They sometimes are beneficial, but usually do not give as good results as we might expect from these vascular antispasmodics. Calcium lactate in 1-gram (15 grain) doses three times daily has been occasionally found helpful. Opium in some cases may be necessary, but it should be used with the greatest caution.

The case presented before you is of considerable interest in that we have two rather rare conditions, scleroderma and Raynaud's disease, combined in the same case. In addition, the patient has a chronic infectious arthritis, an affection which has occasionally been described in association with each of these diseases. McCrae, in his analysis of 500 cases of arthritis, found that there were 11 cases in which scleroderma coexisted with the arthritis, and in 5 of these there was also Raynaud's disease. He comments on the rather striking fact that in no instance did Raynaud's disease occur alone, but always with scleroderma.

CLINIC OF DR. LOUIS HAMMAN

JOHNS HOPKINS HOSPITAL

HYPERTENSION

Its Clinical Aspects

DURING the past winter we have seen in our dispensary clinics a number of patients with hypertension. This symptom has presented itself under a variety of aspects, and I thought there would be some advantage in reviewing the cases and grouping them with this important clinical manifestation as the central point of interest. For this purpose I will present briefly only the important data concerning each patient.

CASE I.—The patient, a young man twenty years of age, came to the dispensary complaining of swelling of the ankles. During the previous month he had had recurring attacks of swelling of the ankles, which would last a few days and then disappear. Just before coming to the dispensary he had noticed a little shortness of breath on exertion. He came to the dispensary particularly because that morning he had noticed besides swelling of the ankles marked swelling of the face. It was interesting that he stated that the evening before he had eaten a large amount of salted peanuts. The patient was pale, and had marked edema of the eyelids and ankles. The heart was possibly a little enlarged to the left; the second aortic sound was ringing, and the blood-pressure was just a little elevated—namely, systolic 150, diastolic 80. The urine showed a very large amount of albumin and numerous casts and a small number of red blood-cells. The patient obviously had an acute nephritis, but it was impossible to say at the time whether it was an acute nephritis alone, or an acute nephritis on top of a chronic process. He re-

mained in the hospital a number of weeks and left unimproved. During his stay in the hospital his blood-pressure was constantly a little elevated.

Case II.—The patient, a colored woman, fifty-seven years of age, married, came to the dispensary complaining of a cold on the chest and nervousness. She dated her symptoms from an attack of grippe she had had a year before. Ever since then she had had cough, and during the three previous months marked shortness of breath. The examination showed a poorly nourished colored woman with marked pyorrhea. The pulmonary examination showed emphysema, with bronchitis and possibly a thickened pleura. The heart was not enlarged. At the apex there was a soft, blowing systolic murmur; the second aortic sound was markedly accentuated. The blood-pressure was: systolic 180, diastolic 135. The vessels were tortuous and their walls considerably thickened. The urine showed albumin and an occasional cast. The specific gravity of the urine varied between 1014 and 1032. The phenolsulphonephthalein test showed an excretion of 50 per cent. in two hours. The Wassermann reaction was negative.

The patient has been coming to the dispensary off and on for the past few months and there has been no essential change in her condition. The diagnosis was hypertension, arteriosclerosis, chronic nephritis (vascular type), emphysema, and bronchitis.

Case III.—The third patient showed a condition very similar to the second. She also was a colored woman, fifty-five years of age, who came complaining of shortness of breath, indigestion, and nervousness. The shortness of breath had been present for three months. Three weeks before coming to the dispensary she had noticed a little swelling of the feet. She had had digestive disturbances and slight giddiness. She was undernourished, and showed as the main clinical findings moderate enlargement of the heart, with a blowing systolic murmur at the apex and marked accentuation of the second aortic sound, with frequent extrasystoles. The urine contained a moderate amount of albumin and many casts. The specific gravity of the two specimens of urine examined was 1010 and 1017 respectively. The phenolsulphone-

phthalein test showed an excretion of 50 per cent in two hours. There was slight edema of the ankles. The eye-grounds showed marked arteriosclerotic changes in the retinal arteries.

The diagnosis was hypertension, arteriosclerosis, beginning myocardial insufficiency. With rest and digitalis the patient's condition was greatly improved.

CASE IV.—The patient, a white man, forty-eight years of age, has been coming to the dispensary off and on during the past eight years. His main complaint has been pain in the shoulders, probably due to a chronic bursitis. During the past three years he has complained of curious cardiac attacks, consisting of extreme palpitation. From their description attacks of auricular flutter have been suspected, but it has been impossible to observe the patient in any of these attacks. The only rhythmic abnormalities that have been found are occasional extrasystoles. For a number of years the blood-pressure has been elevated; the reading on the day he was shown at the clinic was systolic 190, diastolic 120. The heart was a little enlarged to the left and there was a systolic murmur at the apex, with an accentuated aortic second sound. There has never been any evidence of myocardial insufficiency. The urine contained albumin and a small number of casts. The peripheral vessels were tortuous and markedly thickened.

The diagnosis has been myocardial degeneration, hypertension, arteriosclerosis, and auricular extrasystoles.

CASE V.—The fifth patient was a colored man fifty-two years of age, who came to the dispensary complaining of shortness of breath. The examination showed a fairly well-nourished dyspneic negro with marked enlargement of the heart, a gallop-rhythm, edema of the legs, tortuous and thickened vessels, and a blood-pressure of systolic 230, diastolic 135. The urine showed a large amount of albumin and many casts. The patient stated that his symptoms had begun one year before his coming to the dispensary, with polyuria and nocturia. The cardiac symptoms were of only a few months' duration. The eye-grounds showed a marked albuminuric retinitis. The phenolsulphonephthalein output for two hours was 31 per cent. The patient was admitted to the

hospital, where he remained for three weeks and improved somewhat under rest and digitalis treatment. Further tests of renal function showed marked impairment. The test-meal showed a marked fixation of the specific gravity at a low level. There was marked nocturnal polyuria. Ambard's coefficient was 0.159; urea nitrogen 28 mg. per 100 c.c.

Shortly after going home the patient's symptoms returned, and a month or two later he was admitted to the City Hospital.

Case VI.—This patient was particularly interesting on account of his cerebral symptoms. He was a white man, fifty-two years of age, who came to the dispensary in 1914, complaining of paralysis of the right side. Previous to this he had had no important symptoms, and especially no symptoms on the part of the cardiorespiratory apparatus. The loss of power came on very gradually, suggesting a thrombosis rather than a hemorrhage. At that time the heart was normal in size and the sounds clear, except that the second aortic sound was markedly accentuated. The blood-pressure was 240. There was some loss of power in the right arm and the right leg.

The patient has been coming to the dispensary off and on during the past three years, and there has been considerable recovery of power on the right side, but there is still weakness in the right arm and hand, with paresthesias. The blood-pressure when taken has always been well over 200—usually in the neighborhood of 250. The urine has shown a trace of albumin and occasionally a few casts. At present he has the mental slowness that is so common in cerebral arteriosclerosis. His blood-pressure on the day he was shown at the clinic was: systolic 280, diastolic 160. There was still a little weakness of the right arm and hand. The heart was very little, if any, enlarged to the left. There was a systolic murmur at the apex, and the second aortic sound was markedly ringing. The urine showed a large amount of albumin and a few casts. The eye-grounds showed marked tortuosity and narrowing of the retinal arteries.

The diagnosis was arteriosclerosis, hypertension, cerebral arteriosclerosis with thrombosis of a branch of the left middle cerebral artery, chronic nephritis (vascular). There has been

no change in the patient's condition during the past few months.

CASE VII.—The last patient, a white man, thirty-two years of age, came to the dispensary complaining of headache and cramps all over the body. Five years ago he was told that he had kidney trouble. During the period since then he has worked steadily. His main symptoms have been the cramps, which come on principally at night, in the legs and arms. He has also suffered from some headache, and recently shortness of breath on exertion. The examination showed a fairly well-nourished man, very pale and anemic, with swelling of the legs and face. The heart was a little enlarged to the left; a systolic murmur at the apex; the aortic second sound ringing. The arteries were tortuous and thickened. The blood-pressure was: systolic 220, disatolic 170. The eye-grounds showed marked swelling of the disks without albuminuric retinitis. The phenolsulphonephthalein test showed only a trace of the drug excreted during the first hour.

The patient was admitted to the hospital, where his renal function was more thoroughly studied. It showed a maximal involvement. The phenolsulphonephthalein for two hours was 5 per cent. or less; Ambard's coefficient 0.77; urea nitrogen in the blood 97 mg. per 100 c.c. The renal test-meal showed marked fixation of the specific gravity at a low level, namely, 1010 to 1011. There was marked nocturnal polyuria. The urine showed albumin, varying from a very large amount to a trace, and microscopically a few casts.

This patient obviously has a severe chronic diffuse nephritis, probably with secondary contraction of the kidneys.

I may assume that you are familiar with the methods of blood-pressure determination. The palpatory method of estimating the systolic pressure is common knowledge, but I find in my contact with physicians that some have not yet accustomed themselves to use the auscultatory method. The advantages of the latter are very great, since this method permits, with little practice, a reasonably accurate reading of the diastolic as well as of the systolic pressure. The aneroid sphygmomanom-

eters, on account of their convenient size and ease of application, are deservedly popular. In my experience they are accurate and dependable, but it is a wise precaution to have the scale tested from time to time against a mercury manometer. When taking the blood-pressure it is advisable to make a number of readings in quick succession, particularly when the first is unexpectedly high. Once in a while it happens that the first reading is from 10 to 20 mm. higher than the subsequent ones, and when this is the case the first reading must be discarded. This variation is noted mainly in nervous individuals. It concerns the systolic pressure alone, for the diastolic pressure is but little altered or not at all. We now have for our convenience reliable tables compiled from life insurance examinations that show the normal blood-pressure for different ages. As a practical guide one may accept that up to middle life a systolic blood-pressure constantly above 135 mm., and thereafter above 150 mm., is evidence of pathologic hypertension. Unfortunately, we possess no equally satisfactory data concerning variations in the diastolic pressure, and this is regrettable, for diastolic pressures are becoming more and more important in our estimation of hypertension. We have learned that definite and important hypertension may exist even when the systolic pressure is near the normal high level, and that moderate systolic elevation without accompanying diastolic increase is more commonly an indication of some transient influence upon the circulation than of true hypertension. Normally the diastolic pressure equals, roughly, two-thirds of the systolic, and I am convinced that up to middle life a diastolic pressure constantly above 90 mm., and thereafter above 100 mm., is evidence of pathologic hypertension.

An elevation of blood-pressure is observed clinically in a large number of conditions. In many of these hypertension is moderate or transient, and in others the association with a satisfactory primary cause is apparent. This part of hypertension we shall not discuss in detail, and shall merely enumerate the commoner varieties, to bring out more clearly the group we wish to emphasize.

CLASSIFICATION

1. *Hypertension Associated with Increased Intracranial Pressure.*—Cushing has shown that the rise in pressure is due to anemia of the vasomotor center, and he regards it as a compensatory mechanism to furnish a sufficient blood-supply to the medulla.

2. *Hypertension Associated with Asphyxia.*—The rise in pressure is due to stimulation of the vasomotor center by the excess of carbon dioxid. Clinically, similar elevations are found in bronchial asthma, laryngeal stenosis, and, less strikingly, in cardiac disease with broken compensation.

3. *Hypertension Associated with Intoxications.*—The best known varieties are:

(*a*) Hypertension in eclampsia.

(*b*) Hypertension in lead-poisoning.

(*c*) Hypertension in anuria.

4. *Hypertension Associated with Nervous Disorders.*—Under the influence of pain, fear, and other emotional states the blood-pressure is often temporarily elevated. Usually the elevation concerns only the systolic pressure, the diastolic remaining at the normal level. Neurasthenic patients are susceptible to such transient hypertension.

5. *Paroxysms of hypertension*, usually associated with severe symptoms, such as angina pectoris, dyspnea, pulmonary edema, abdominal pain (Gefässkrisen of Pal). Such paroxysms occur usually as marked but brief elevations of pressure in patients with permanent hypertension.

Excluding these varieties of hypertension, for the most part transient, there remains the commoner type in which hypertension is marked and permanent, and assumes a prominent and often predominating part in the clinical picture.

Chronic hypertension is pre-eminently a symptom of middle life and later years. It occurs more commonly in men than in women. The blood-pressure is usually 180 mm. of mercury or over. It is observed in three clinical forms.

1. A benign form, in which hypertension and its consequences are for a time at least the sole clinical manifestations.

2. A malignant form, in which hypertension is the expression of a progressing chronic diffuse nephritis.

3. An intermediate form, in which there is a varying amount of renal involvement due to vascular and not to inflammatory changes.

The benign form of hypertension is frequently encountered in the course of a routine examination, the patient not complaining of symptoms referable to the high blood-pressure. Many of the cases are discovered by the life insurance examiner. When symptoms induce patients to seek medical aid they complain usually of dyspnea on exertion, palpitation, precordial distress, angenoid pain, headache, vertigo, fatigue, or, ill-defined, so-called neurasthenic symptoms. The examination reveals, besides hypertension, cardiac hypertrophy and perhaps slight dilatation of the aortic arch. In cases of long standing the peripheral vessels are tortuous and thickened. The urine is usually normal, may contain a trace of albumin and an occasional hyaline cast, but appropriate tests show unimpaired renal function. The late symptoms are associated with myocardial insufficiency or with cerebral vascular accidents. When observed before the onset of myocardial insufficiency the prognosis is good, for many patients live ten or fifteen years and longer after the discovery of hypertension. I have strongly impressed upon my mind one such instance. In 1907 the patient, a man then forty-eight years of age, consulted me on account of oppression in the chest and attacks of dizziness. The heart was hypertrophied but not dilated, the peripheral vessels diffusely thickened, the blood-pressure: systolic 220 mm., diastolic 140 mm. The urine contained at times no albumin, at other times a faint trace, and occasionally a few hyaline casts were discovered. The specific gravity varied from 1007 to 1023. Impressed by the gravity of the situation, I advised a rigid readjustment of the patient's life, but, although he admitted the wisdom of the advice, he never brought himself to follow it. During the past ten years he has remained actively engaged in directing the affairs of a large corporation, and is apparently as well now as he was when I first examined him. On a number of occasions during this

period I have had occasion to take his blood-pressure, which has always been in the neighborhood of 220 mm.

The malignant form of hypertension associated with chronic diffuse nephritis may usually be recognized by the obvious evidence of renal disease. The illness begins with urinary symptoms. If the patient comes under observation after myocardial insufficiency has developed the heart manifestations may dominate the clinical picture, but, as a rule, careful inquiry will elicit a history of antedating nocturia and polyuria. In these cases examination reveals, in addition to arterial hypertension and its accompaniments, definite evidence of renal involvement. The urine contains a relatively large amount of albumin, casts are numerous, and there may be polyuria, with a constantly low specific gravity. Appropriate tests, such as the phenolsulphonephthalein test, will demonstrate a reduction of renal function. In the late stages of the disease anemia often develops. Retinal changes and hemorrhagic areas of exudate are frequently found, and may be discovered before other symptoms have impressed us with the gravity of the condition. Striking examples of this nephritic type of hypertension are seen in patients with kidneys contracted secondarily to a subacute or chronic nephritis. The prognosis is much more serious than in benign or essential hypertension. Patients seldom live over three years after the diagnosis is made, and sometimes the symptoms progress with amazing rapidity, so that death arrives within six months after the onset of hypertension. The final symptoms may be due to uremia, to myocardial insufficiency, or to cerebral accidents, and, indeed, are frequently caused by a combination of two or three of these conditions.

The third, or intermediate form, of hypertension is the commonest clinical type. The group shades off imperceptibly into the essential or benign group; it is better but by no means sharply demarcated from the nephritis group. The early symptoms are those of the essential form. Symptoms of renal insufficiency, if they develop at all, come later in the course of the disease.

This rough classification is helpful, I think, in studying our cases, and also has some bearing upon treatment, but it

must not be understood to imply a rigid separation into clinical types, and still less a strict anatomic distinction. A patient may come under observation today and apparently belong to the group of essential hypertension; a year later further evidence may prove that he had really a chronic diffuse nephritis. In the course of years a vascular nephritis may be added to what was at first an essential hypertension. Not infrequently inflammatory changes occur in kidneys with vascular lesions, and combined forms of nephritis develop. Thus arise clinical pictures of great diversity. It is possible to draw a relatively sharp distinction between hypertension associated with chronic diffuse nephritis and other forms of hypertension. In most instances the evidence of nephritis is clearly marked in the former group of cases. I am speaking now of patients with hypertension unaccompanied by myocardial insufficiency, for I shall later refer to the insurmountable difficulties that are encountered in attempting to draw this distinction after the heart failed to carry on the circulation adequately. The age of the patient is an important element, for hypertension developing under forty is nearly always associated with a chronic diffuse nephritis. A large amount of albumin and numerous casts in the urine point in the same direction. Albuminuric retinitis, as distinguished from the retinal changes due to arteriosclerosis, is a further important indication. Finally, well-marked evidence of impaired renal function is often decisive. The distinction between the essential and the intermediate types of hypertension is not so sharp; one group shades off imperceptibly into the other. The distinction exists mainly in the presence or absence of evidence of renal involvement, indicated by the occurrence of albumin and casts in the urine and some reduction of renal function.

NATURE OF HYPERTENSION

Unfortunately, no matter what terms are selected with which to speak of hypertension the implication of these terms draws one, be he ever so unwilling, into the fruitless consideration of the nature of hypertension. The term "nephritic hypertension" implies a conviction that hypertension is sometimes caused by

renal lesions; "arteriosclerotic hypertension," that arterial changes may be the cause of high blood-pressure; and "essential hypertension," that the increased pressure may occur as a manifestation of some functional derangement independent of anatomic change. There is nothing so firmly established about hypertension as the unquestioned relation to nephritis. Long before the use of blood-pressure measuring instruments clinicians had discovered their frequent association. However, there are few today who hold the extreme view that kidney changes are the sole cause of hypertension. As you know, this view has been strongly championed and many attractive arguments have been offered in its favor. That some instances of hypertension are purely functional has been established by rigid postmortem studies, and that vasomotor influences play an important, even though it may be a secondary, part in hypertension is guaranteed by the marked and rapid changes in pressure so frequently observed. Arterial changes are always found when hypertension has been present a long time; the arteries are thickened and tortuous. However, we are still unable to decide between the conflicting views that regard the arterial changes on the one hand, as the cause of the hypertension, and on the other, as its result. Of this much we are certain, arteriosclerosis in the sense of a degenerative disease of the arterial walls has no relation to hypertension. Daily we see old people with calcified, almost incompressible arteries and a normal blood-pressure. If arteriosclerosis is accepted as a cause of hypertension, then we must look upon the arterial disease as different from the senile, degenerative changes. It is, more properly speaking, an arteriolar sclerosis, an arteriocapillary fibrosis. The arteries in the early stages show great thickening of the muscular coats—a condition that has been interpreted by many as indicating hypertrophy from long-continued overfunction. Later, fibrous changes become evident, and finally secondary degenerative sclerosis may occur.

TESTS OF RENAL FUNCTION

In the differentiation of clinical types of hypertension I have put stress upon the estimation of the degree of renal involve-

ment. The urinary examination for albumin and casts is important, but alone it does not serve our purpose. We must, in addition, determine the functional capacity of the kidneys. A complete and thorough study of renal function has become an elaborate and exacting discipline. The practising physician cannot determine the Ambard coefficient of urea excretion, the nitrogen partition in the blood and urine, the salt metabolism, nor use the many other helpful and intricate tests that have been proposed. Thorough study of these methods is daily advancing our knowledge of renal function, and, fortunately, we have already learned a few very simple and highly satisfactory tests that meet the practical requirements of yielding the maximum amount of information from the minimum amount of time and trouble. The two methods that have measured up best to this rough practical standard are the phenolsulphonephthalein test and the study of the quantitative urinary output and its specific gravity.

The *phenolsulphonephthalein* or, as it is colloquially called, the *phthalein test* is the simplest and most valuable of all the tests of renal function. One c.c. of the dye is drawn from the ampule into a sterile syringe and injected under the skin of the patient. One hour and ten minutes after the injection a specimen of urine is collected, and one hour later, a second specimen. The amount of the dye excreted in these specimens is estimated separately by making them alkaline with sodium hydroxid and diluting them to 1 liter and comparing the color with a standard solution containing 1 c.c. of the dye in 1 liter of water. The comparative readings may be made very accurately by a simple method that I have used with entire satisfaction for a number of years. No special apparatus is required; only a buret, a 5-c.c. pipet, a 1-c.c. pipet graduated in tenths, and a few test-tubes are needed. If the test is made only occasionally it is advisable to make up a fresh standard for each test. The ampules used for the injection contain a little over 1 c.c. of the phthalein solution, so that after the injection has been made enough remains to make the standard by measuring 0.1 c.c. in a pipet and adding this to 100 c.c. of water made alkaline with a little sodium hydroxid. From a

number of test-tubes two are selected of equal caliber. The caliber is estimated by adding to the tubes 10 c.c. of water and choosing two in which the water rises to a corresponding level. Into one of the tubes put 5 c.c. of the standard solution; into the other 5 c.c. of the diluted urine, made alkaline with sodium hydroxid. The correct percentage of phthalein in the urine is obtained by diluting the urine to 1 liter; but in performing the test the degree of dilution must be varied to suit the particular specimen. If the urine is highly colored by the dye it may be diluted at once to 1 liter; if there is less color it is better to dilute to 500 c.c.; if there is little color, to only 250 c.c. In the first instance the correct reading is obtained at once; in the second the result must be halved; in the third it must be divided by four. To the standard solution water is added from the buret until the color matches that of the diluted urine. The percentage of phthalein in the urine will then equal the sum of the number of cubic centimeters of standard solution employed plus the number of cubic centimeters of water added from the buret, divided into the number of cubic centimeters of standard solution employed. A control reading may at once be made by adding 5 c.c. of water to the 5 c.c. of diluted urine, thus doubling the dilution, and continuing the addition of water from the buret to the standard solution until the colors again match. For instance, the specimen is made alkaline and diluted to 500 c.c.; 5 c.c. of this filtered specimen is put into one test-tube; into the other 5 c.c. of the standard solution. It requires 3 c.c. of water to bring the standard solution to the same color as the diluted specimen; the percentage of phthalein in the urine will then be $\frac{5}{5+3} = 62.5 \div 2 = 31.2$ per cent.; 5 c.c. of water are now added to the 5 c.c. of diluted urine, raising the dilution from 500 c.c. to 1 liter; water is again added from the buret to the standard solution until the color matches that of the diluted urine. It requires in all 10.5 c.c. of water to bring the standard solution to the same color as the diluted specimen; the percentage of phthalein in the urine will, therefore, be $\frac{5}{5+10.5} = 32.2$ per cent. The two readings agree so closely that 32 per cent. may be accepted as accurate. Normally the phthalein output for two hours is 60 per

cent. or over. An output from 50 to 60 per cent. represents a slight, almost a negligible, impairment of function; from 40 to 50 per cent., a moderate but definite impairment; from 20 to 40 per cent., a marked impairment; from 10 to 20 per cent., a serious impairment; and below 10 per cent., a critical impairment.

The test of renal function by *estimating the urine output* and the *variation of its specific gravity* is as simple as the phthalein test. It is merely an elaboration of the well-known clinical facts that kidneys with impaired function lose their ability to secrete a concentrated urine and that the polyuria associated with the disturbance is particularly noticeable at night. The test consists in collecting frequent specimens during the day and measuring their specific gravity, and in comparing the quantity of urine passed during the day with the quantity passed during the night. The patient is instructed to take liquids only at meals and to pass the urine every two hours during the day, beginning at 8 or 9 o'clock in the morning. The last specimen should be passed at least two hours after the evening meal, and no fluid must be taken after the meal. The urine passed during the twelve night hours may be collected as one specimen. The amount and the specific gravity of each of the seven specimens are determined. In normal persons, when no excess of fluid is taken, the night urine never exceeds 450 c.c.; any amount above this indicates a nocturnal polyuria. Normally specific gravity of the urine varies greatly, but at some time of the day it will reach 1020 or over. Kidneys unable to secrete a urine of a concentration of 1020 show a disturbed function. A constantly low, fixed specific gravity indicates seriously impaired function.

The practical value of these two simple tests cannot be overstated. Applied to the study of hypertension they are invaluable for denoting the degree of renal impairment. Like most other tests they must be interpreted with reasonable precaution. The most important disturbing element in their interpretation is the presence of myocardial insufficiency. In hospital practice many, indeed most, cases of hypertension come under observation after serious symptoms have developed, and

since these symptoms are commonly associated with a failing circulation, a true estimate of the degree of kidney involvement may be difficult and often impossible. Under these conditions renal function is seriously impaired by the venous stasis, and the urine may be highly albuminous and contain abundant casts, and the phthalein output be greatly reduced in the absence of any real kidney disease. The polyuria associated with a disappearing edema may completely upset our calculations based upon the amount and the specific gravity of the urine. If appropriate treatment succeeds in re-establishing the circulatory balance, albumin and casts may disappear from the urine and the phthalein output become normal.

PROGNOSIS

I have put much emphasis upon the separation of hypertension into different clinical types, and in order to justify the emphasis I must show that the distinction bears important practical consequences. Our knowledge of the cause of hypertension is so meager and our skill in treating it so limited that for the present at least the main practical value of the distinction is for purposes of prognosis. However, in this respect the value is undisputed. Hypertension itself is not the grave and serious malady it is commonly taken to be. As an isolated symptom it is compatible with many years of enjoyable and useful life. It is very wrong to harass patients with the fear and anxiety a knowledge of the condition often evokes. I am as keen as another for an honest and open understanding between physician and patient, but I abhor the too common practice of impressing the blood-pressure with accurate figures, and of leading, or at least allowing, the patient to gage his condition and his fate by slight variations in occasional readings. The type and the degree of renal involvement is the most important factor in prognosis. A chronic diffuse nephritis is nearly always a steadily, even though it may be a slowly, progressing disease. A vascular nephritis with little or no disturbance of renal function has not nearly so serious a significance. A pure hypertension without any evidence of renal involvement offers, other conditions being

equal, the best prospects for many years of relative well being. I need merely repeat that in many instances it is difficult, and in some cases impossible, satisfactorily to separate individual patients according to any proposed classification.

SYMPTOMS OF HYPERTENSION

Properly speaking, there are no symptoms characteristic of hypertension; the symptoms that so commonly develop with it are usually due to associated changes in important organs. The headache, the lassitude, the weakness, the vague neurasthenic symptoms that patients with hypertension frequently complain of, are not necessarily the direct evidence of hypertension. Headache, one of the commonest of these symptoms, is often too lightly dismissed as a result of the high blood-pressure. I have seen many instances in which this ready interpretation has stood in the way of fuller investigation and thus led to important data being overlooked. I remember one such instance very clearly. A lawyer, fifty-four years of age, after a long period of arduous work upon an important and difficult case began to have headache and severe pain in the neck at the base of the skull. The examination revealed hypertension, and therapeutic measures were directed toward the alleviation of this condition. Rest, diversion, massage, electricity, baths were successively employed without giving relief. He spent a year in a sanatorium without benefit. At the end of this year he felt that everything had been tried, that all treatment was unavailing, that he was an invalid doomed to fret out his remaining days in inactivity and misery. An *x*-ray examination revealed a definite osteoarthritis of the cervical vertebræ; a number of badly infected teeth were extracted, and the distressing symptoms quickly disappeared. For two years now the patient has been working actively and happily at his profession, undisturbed by the hypertension that no doubt persists. I quote this one instance as a warning to you not to fall into the prevalent habit of ascribing to the hypertension all of the symptoms of which a patient with high blood-pressure may complain. It is important to remember that before the onset of complications hypertension frequently,

indeed, I should say in the majority of instances, gives the patient no warning of its presence.

The complications that most often give rise to symptoms in hypertension affect chiefly the kidneys, the heart, and the nervous system.

I mention the kidney first not because symptoms on the part of that organ deserve the chief consideration, but because in view of what has already been said, they may quickly be disposed of. In chronic diffuse nephritis the renal changes are not a complication of hypertension, but represent the primary factor in the sequence. Grave renal insufficiency, with its well-known symptoms, frequently occurs in this condition, but it would be a mistake to conclude that it invariably dominates the clinical picture. Often serious cardiac manifestations come on before functional impairment of the kidney has advanced far enough to cause important symptoms. In essential or primary hypertension associated with arteriocapillary fibrosis symptoms of renal insufficiency occur much less often. They seldom obtrude as the dominating symptom except when inflammatory lesions are superimposed upon the vascular, or when the vascular lesions are followed by marked contraction. The urinary symptoms, suggesting marked renal involvement, that is, abundant albumin and casts, are more commonly due to myocardial insufficiency than to extensive kidney disease.

The heart more commonly than any other organ shows symptoms in hypertension. It usually presents the earliest symptoms; it often holds our first attention throughout the illness, and cardiac failure is the most frequent cause of death. Cardiac failure in hypertension is occasioned by two factors. The first and in many instances the most important of the two is the increased resistance against which the heart must work. As a result of this increased resistance the left ventricle hypertrophies, the second aortic sound acquires a sharp, ringing quality, and the aortic arch is often a little dilated. It is worth emphasizing that the left ventricle may be greatly hypertrophied without there being any marked enlargement of the area of cardiac dulness. When the percussion outline of the heart is decidedly

altered, dilatation has been added to the hypertrophy, and with this objective evidence of myocardial weakening are usually associated obvious symptoms of circulatory insufficiency. The stress of hypertension falls first upon the left ventricle alone; when the chamber dilates a relative mitral insufficiency is produced, and consequent upon this the right ventricle also hypertrophies and dilates. Not infrequently when myocardial insufficiency is well marked a typical picture of relative tricuspid insufficiency is presented. The second factor in cardiac failure is the condition of the heart muscle. We by no means fully understand all of the conditions that influence the efficiency of the heart muscle. Why does a heart that has for years struggled successfully against an overwhelming burden suddenly give way and fail in its task? To say that the heart weakens after long-continued overstrain does not explain the mechanism of the weakening. However, although we cannot explain this mechanism in detail, still numerous observations convince us that hearts vary greatly in their resistance to overwork. Some play out more quickly than others. No doubt there are inherent differences in the heart muscle of different individuals; general metabolic and nutritional disturbances must play an important rôle, as witness, for instance, the influence of anemia; the effects of infection are well known; and lastly, local circulatory disturbances in the heart itself are factors of the first importance. Whether the arterial changes associated with hypertension be primary or secondary, the localization of these changes in a very large measure determines the predominating symptoms. I have spoken of the kidney changes due to marked sclerosis in the renal arteries; in a few minutes I shall refer to the dramatic symptoms accompanying extensive sclerosis of the cerebral vessels; and at present I wish to emphasize the equal importance of these changes in the coronary circulation. In many instances the condition of the coronary arteries decides the resistence of the heart muscle and is largely responsible for the early development of myocardial insufficiency, as well as for many of the other less common cardiac symptoms.

The third important group of symptoms that arise in associa-

tion with hypertension are due to vascular lesions in the central nervous system. With these you are all familiar. Symptoms due to alteration in the arteries of the spinal cord are so uncommon that they deserve only mention. Of the cerebral vessels, hemorrhage and thrombosis affect chiefly the middle cerebral arteries, producing hemiplegia, aphasia, and unilateral sensory disturbances. Less common and more complicated pictures are occasioned by vascular lesions in other regions. Our interest is particularly attracted by the transient cerebral symptoms so characteristic of cerebral arteriosclerosis. A patient may momentarily forget his name; a more complete aphasia may last for a few minutes or longer; a hemiplegia or a monoplegia may clear up completely in a few hours or a few days; curious mental states come on that quickly pass off without leaving a mark of their stay. The nature of these transient attacks is obscure. It is tempting to explain them as the symptoms of a temporary spasm of the cerebral arteries, but careful observation makes it more and more evident that in the majority of instances they are due to definite focal lesions.

I have not exhausted the symptomatology of hypertension. Arteriosclerotic changes in still other organs are associated with interesting and characteristic symptoms. In the splanchnic area particularly important manifestations arise. However, time presses, and I must be satisfied to emphasize the commonest and most important symptoms, and especially those that have been prominent in the cases we have observed.

TREATMENT

In the few remaining minutes I have time for only a few words about treatment. Perhaps a few words will be sufficient, since we are now taking a broad oversight of hypertension and cannot stop to consider complications and their treatment in detail. I have intimated that we lack any precise and demonstrable explanation of the nature and cause of hypertension, and I wish to preface my remarks on treatment by restating and emphysizing this deplorable ignorance. As is usual in obscure departments of medicine, the absence of definite knowledge

incites to boundless speculation, and the further such speculation is removed from the reach of searching scientific inquiry, the more tenaciously it is held and the more dogmatically affirmed. At present auto-intoxication and, more particularly, protein intoxication hold the stage. It is often difficult to realize when reading some plausible exposition of its rôle that the deductions rest upon fancy and not upon sound facts. For all we know some form of intestinal intoxication may play an important part in the production of hypertension, but as yet there are no observations to support this view, much less to enforce it, and for the present it is better not to prejudice our judgment with unfounded views. Being ignorant of the exact cause of hypertension we cannot formulate a precise method of prevention or treatment. However, empirically we have accumulated certain impressions which may temporarily guide us, since they rest upon suggestive though not convincing observations. Let me say that I omit from this discussion all consideration of hypertension associated with chronic diffuse nephritis. The problem here is the treatment of the nephritis and, secondarily, of the complications induced by the hypertension.

The view that hypertension is a compensatory mechanism and that it is a valuable defense reaction has gained general acceptance by the profession. In harmony with this view the use of vasodilating drugs has been tremendously reduced. Nitroglycerin, amyl nitrite, sodium nitrite, and erythrol tetranitrite are now used almost exclusively for temporary effect. Employed to meet special conditions they are of great value, but it is no longer regarded as good practice to prescribe the nitrites whenever the blood-pressure is found high. Aside from any theoretic consideration there are practical consequences that confirm this usage. In the first place, experience teaches that the continued use of the nitrites has no effect upon the general course of the disease, and in the second place a vigorous administration of the nitrites, so as to produce a marked fall in pressure, may be followed by serious symptoms. Occasionally anuria with threatening uremia may result. Potassium iodid is still a popular remedy. It is questionable, however, whether it has

any decided influence upon the symptoms except in cases complicated by a luetic aortitis.

In a chronic disorder in the course of which symptoms vary, often apparently spontaneously, at other times in response to unforeseen accidents, it is difficult to estimate the effects of treatment. The methods that we now employ seem to yield a definite measure of success, even though this success cannot be convincingly stated. We believe that the best results are accomplished by an orderly regulation of the patient's life and by protecting him from deleterious influences. Our therapeutic endeavors are based upon the belief that the heart, the arteries, and the kidneys are injured by (1) physical and mental, especially emotional, overexertion; (2) excessive demand upon metabolic processes, and (3) infections. I shall therefore speak briefly of occupation, exercise, diet, and infections.

The regulation of a patient's occupation is one of those delicate adjustments that require the application of common sense more than of medical knowledge. I have learned, just as you will learn, many a costly lesson. You cannot take a man who has spent his life in the busy turmoil of affairs and suddenly cut him off from all his interests and occupations. He has nothing to live by or live for. Few such men have developed outside interests that are sufficiently stimulating and occupying to fill the day with happy contentment. The adjustment calls for a compromise between the character and tastes of the particular patients and the demands of medical practice. Each patient is an individual problem. It is usually possible with a little patience and encouragement gradually to eliminate the irksome worries and cares of business while preserving a reasonable amount of interest in its management.

Of exercise I need only stop to say that the amount must be rigidly regulated by the condition of the heart. In patients with a delicately adjusted cardiac balance a single overexertion may precipitate myocardial insufficiency, with a serious and even fatal chain of symptoms. On the other hand, in robust men under fifty, with hypertrophied hearts that easily manage the increased resistance, carefully graduated exercise is often decidedly

beneficial. When a reduction of weight is desired a reasonable amount of exercise is often desirable. Less vigorous patients are often aided by passive movements and mild gymnastic exercises.

Diet regulation is important in two ways: (1) to reduce the metabolic demands to a minimum; (2) to eliminate harmful foods. Hypertension is commonly found in persons who habitually overeat and in the obese. It occurs mainly after middle life, and the actual dietary demands of well-being at that age are surprisingly small. Next to the prevention of infection a resonable regard for the weight of the patient is the most valuable service we can render. As I have pointed out, the heart bears the main brunt in hypertension, and whatever we can do to lighten the burden upon that organ demands serious attention. We need not aim to bring all patients to an optimal standard of weight, but obesity adds a burden of such importance to the circulation that a carefully regulated reduction should often be the principal object of treatment. I say "carefully regulated" because brusque and rigorous reduction cures must be avoided. I cannot stop to analyze the data upon which rest our impression that protein, and meat in particular, is harmful to patients with hypertension. I can only say that a general impression of its harmfulness is firmly established, and in accordance with this view it is customary to devise a diet low in protein, with meat completely eliminated or nearly so.

And finally I have left for the last what I regard as the most pressing therapeutic problem in hypertension, namely, the prevention of infection. How common it is, how very common, to see serious cardiac or renal symptoms ushered in by an apparently trivial infection. The heart or the kidney, as may be, carries on its work with a satisfactory functional range, and then abruptly fails to meet the usual demands when an inflammatory or toxic lesion robs it of its last reserve. As a part of the regular therapeutic program foci of infection must be diligently searched for, and, if found, appropriately treated. The patient must also be guarded as far as possible from exposure to the common respiratory infections. How such a guard shall be established depends upon the susceptibility and the circumstances of the patient.

TWO UNUSUAL CASES

1. Dermoid Cyst of the Mediastinum. 2. Milroy's Disease.

DERMOID CYST OF THE MEDIASTINUM

I FEEL that I owe an apology for presenting the following two patients. Each represents a very unusual condition, and it is possible that some of you may never be called upon to recognize the disease. However, occasional encounters with rare clinical anomalies sharpen our interest in the more commonplace conditions, and by contrast help to fix the characteristics of the latter more firmly in the mind.

The first patient is a white man, thirty years of age, who came to the hospital in February, 1914, complaining of cough and expectoration. At that time the history showed nothing of importance in the family record, and in his past history the only point of interest was that he had had asthma at the age of six years, which stopped when he had typhoid fever a little later. From that time up to the onset of the present illness he had remained well.

Present Illness.—In 1910 the patient took a deep cold, and this was followed by pneumonia in the right chest, from which he completely recovered. The following year he had a second attack of what was called pneumonia, and during this illness he had a high fever, sweats, pleural pains, chills, and great difficulty in breathing. In 1913 he had a third attack of pneumonia, and during this attack coughed up a large amount of green fluid, mixed with blood. After this last attack, that is, in the fall of 1913, he was sent West, with a diagnosis of pulmonary tuberculosis, although no tubercle bacilli were found in the sputum. He remained at a sanatorium in Colorado for six or eight months. During this period he had a number of hemoptyses. He was examined very thoroughly by the physicians at the sanatorium, who were never able to find tubercle bacilli in the sputum.

They were convinced that he did not have pulmonary tuberculosis and thought that he possibly had a tumor. He returned East in February, 1914, and came at once to the hospital.

The examination at that time showed a sparely nourished young man with a sallow complexion. The mucous membranes, however, were of good color. He did not look to be very ill. The general examination showed nothing of importance except findings in the chest. The chest was fairly well formed, the costal angle about 90 degrees. There was definite fulness in the left upper front with limitation of movement. Over the right side of the chest the note was everywhere resonant and the breath sounds vesicular and clear. Over the left front there was a little impairment above and below the clavicle down to the fourth rib, and a definite area of flatness beginning at the upper border of the second rib and extending from the left border of the sternum 6½ cm. to the left in the third interspace and down to the fourth rib. Over the area of impairment the breath sounds were greatly diminished in intensity, and just along the border of the sternum there was definite tubercular breathing with whispering bronchophony. After coughing, numerous bubbling râles were heard over the area of impairment, extending out to the anterior axillary line. In back there was a little impairment in the left supraspinous fossa, where the breath sounds were diminished in intensity. During his stay in the hospital the patient had a great deal of cough, with profuse mucopurulent expectoration. The sputum showed small bits of elastic tissue, but tubercle bacilli were never found. Bronchoscopic examination showed a thick purulent discharge coming from the first branch of the left bronchus, and no pus from any point below this opening. The Wassermann reaction was negative. The temperature during the two weeks he was in the hospital ranged from about 98° F. in the morning to 101° F. in the evening. The condition at that time excited a great deal of interest, but no definite diagnosis was made. The impression that I dictated after examining the patient was as follows: "The physical examination gives the impression of there being a mass in the mediastinum, pushing out to the left and compressing the lung, rather than of a disease of the

lung itself. The principal possibilities are a mediastinal abscess or a dermoid cyst which has ruptured into the bronchus."

The history of pneumonia and the symptoms following so directly upon it led me to believe that the former of the two conditions was the likely one. I was so much interested in the patient that I had him report to me after he left the hospital, and since then I have had the opportunity of going over him about twice a year. Up to the past year the conditions remained the same. His general health was unaltered—indeed, he gained somewhat in weight. During these three years he has on a number of occasions had rather severe hemoptysis. In March, 1916, he noticed for the first time that there were a few hairs in the sputum, and since then he has noticed hairs in the sputum on a number of occasions. He has brought with him for verification a number of hairs that he has taken out of the sputum. These, as you see, are rather long, thin brown hairs, the longest measuring about 15 cm. He weighs a little more now than he did when he was in the hospital three years ago and his color is better. Otherwise the physical examination shows exactly the same conditions as were present in February, 1913.

With the occurrence of hairs in the sputum a diagnosis is definitely established. The patient has, of course, a mediastinal dermoid cyst, situated in the upper anterior portion of the mediastinal cavity, compressing the left upper lobe. The history of his illness is quite characteristic of the condition, and had I been familiar with the literature I think the diagnosis could easily have been made before hairs appeared in the sputum.

There are two excellent summaries of the condition in the literature, one by Morris in the *Medical News* for 1905, and one by Dangschat in the *Archiv für klinische Chirurgie*, 1903. Morris collects and analyzes 56 cases. The disease affects males and females about equally. Although the tumor must, of course, be present from birth, it seldom gives rise to symptoms until after puberty. Curiously enough there is a tendency for the tumor to grow and produce symptoms shortly after puberty. Over 50 per cent. of the cases first give symptoms between the twentieth and thirtieth year. Some cases have been discovered before the

tenth year, and in 4 cases symptoms were postponed until after the fiftieth year. The cysts are located most commonly in the anterior medastinum and are usually situated beneath the upper half of the sternum. They usually extend to one or the other side, and if they extend to both sides then they lie mainly to one side. They vary in size from tumors as small as a walnut, which are discovered accidentally at autopsy, to masses as large as a child's head, containing as much as 3 liters of fluid. The walls are commonly thin, but may be considerably thickened by inflammatory changes. Dense adhesions are always present, making extirpation very difficult and often impossible. The inner lining of the cysts usually resembles skin and has numerous polypoid (?) excrescences. In the walls, bone, cartilage, teeth, glands, and other structures are frequently found. Nearly all of them contain hair. In nearly half of the cases the cysts have ruptured into a bronchus. Less commonly they have ruptured into the lung, into the pericardium, into the aorta, into the pleura, into the vena cava, and externally through the skin.

The symptoms are extremely varied. Sometimes the mass is discovered before serious symptoms have developed; at other times, when the early symptoms are associated with rupture of the cyst, grave manifestations may appear abruptly. The chief symptoms that occur are dyspnea, pain, pleural effusion, cough, and sputum. Three of the reported cases have been associated with pulmonary tuberculosis, making the diagnosis extremely difficult. A number of the patients have had febrile attacks similar to those of which our patient complained. Hemorrhages are very common occurrences, and at times are large. The sputum is usually large in amount and sometimes has a foul odor. In 10 instances hair was discovered in the sputum, in 7 of the 10 leading to the correct diagnosis. Occasionally horny epithelial cells, fat droplets, and cholesterin crystals may be found in the sputum and give the clue to the correct diagnosis. After symptoms have once developed the disease usually progresses rapidly, and death occurs, as a rule, within four to five years. Death has followed within two or three months of the development of symptoms, and in one case

the symptoms lasted for forty-four years. The physical signs are those usually associated with tumor in the mediastinum. In a number of instances the cyst protrudes above the clavicles. When the cyst is very large, and particularly when it is situated in the posterior mediastinum, it may simulate a pleural effusion. After rupture has occurred the signs may be very confusing and lead to great difficulty in diagnosis. In 5 of the reported cases the dermoid cyst underwent malignant degeneration.

When one is familiar with the symptoms of this conditon the diagnosis can easily be made. When hair occurs in the sputum its significance is obvious. Not finding hair, the presence of horny epithelial cells, of fat droplets, and of cholesterin in the sputum would furnish conclusive evidence. Dermoid cysts may be distinguished from malignant disease by their longer duration and the absence of cachexia. Pressure symptoms are more common with malignant disease than with dermoids. The favorite age of incidence of dermoid cysts is under thirty; of malignant disease, over thirty. Aneurysm also, as a rule, occurs at a later age. The pressure-symptoms again would serve to distinguish the two. The Wassermann reaction would also be helpful. Large dermoid cysts may be differentiated from pleural effusion with difficulty. One of the most confusing possibilities is encapsulated empyema. Constitutional symptoms are often present, and these may lead to the suspicion of a mediastinal abscess. However, a localized abscess in the mediastinum is a very unusual condition. The history would serve to distinguish the two, although in our case it led to confusion.

The **prognosis** is always grave, and the condition is invariably fatal unless the patient dies from some intercurrent disease. Occasionally patients live a long time after the development of symptoms, but it is rare for symptoms to last over ten years. The only available **treatment** is surgical interference. Twenty of the reported cases have been operated upon, and 14 of the 20 survived the operation, with improvement or cure. In one reported instance the whole tumor was successfully removed. In most instances the cyst was incised and drained.

The question of operation and the chances of a cure have been fully explained to this patient, and he is now taking the matter under consideration. The severe hemorrhages that he has had during the past year make the prognosis very grave unless an operation is performed. The tumor is very favorably situated for operation, and I hope that, understanding the advantages and at the same time the possible dangers of this method of treatment, the patient will consent to having the operation performed.

MILROY'S DISEASE

The second patient, a boy fourteen years of age, came to the dispensary last summer complaining of swelling of the right leg. In August, 1915, he fell from a wagon and thinks he must have injured his right leg. There was no pain at the time, but the following night the leg began to swell and got very red, and the patient was unable to walk for ten days. The swelling persisted for three weeks and then gradually went down, although the leg never went back to its previous normal size. Ever since it has been a little swollen. In June, 1916, the boy again injured the leg. The accident, as on the first occasion, was a trivial one. Following the accident there was no evidence of injury, but the leg became inflamed and swollen, and he was unable to use it for some time. Again the swelling decreased, but the leg has permanently remained a little swollen. The examination on July 11th showed a well-nourished boy, rather short for his age, but stocky and well built. The legs and arms were rather short and the hands and feet a little pudgy. There was a congenital ptosis of the right lid with a tendency to external squint of the right eye. The boy showed marked retardation of mental development.

The general physical examination showed nothing of importance except the condition of the legs. The lungs, the circulatory and the abdominal organs were all normal. The urine showed no abnormality. The right leg was swollen to about twice the size of the left, the swelling being almost entirely below the knee. The edema was very firm and brawny, suggesting lymph stasis rather than venous stasis. The leg was not red nor hot. There

was just a little pitting of the left ankle. The eye-grounds showed nothing remarkable.

The patient, then, presented the remarkable condition of a persisting brawny edema of the right leg without any systemic abnormality to account for it. Since that time he has come to the dispensary off and on, and the size of the leg has gradually decreased, but has never completely receded. He gets about very comfortably by wearing a tight bangage on the right leg. During the winter the father of the boy came to me with the request that I see the mother, who was suffering, so he said, from a condition very similar to that which had affected the boy during the summer. He added that she had been having attacks of swelling of the legs for over twenty years, and that her legs were always a little swollen. I went to see the boy's mother, a woman of about forty-five years of age. She said that about four years before she had had a chill with fever and that her right leg immediately became very red and hot and began to swell. She had had such attacks off and on for twenty years, and the swelling of the leg was always preceded by chills and fever. Between the attacks there was always a little remaining swelling, but she got on very comfortably by wearing a bandage. When I saw the mother her leg was greatly swollen—at least to three or four times the size of the other leg. It was very red and hot and there were numerous red stripes over it that looked like inflamed lymphatics. The edema was extremely brawny, and the whole picture suggested very strongly a generalized lymphangitis of the leg. There are no other definite cases of this remarkable condition in the family except that the mother states that one of her sisters has a similar condition. There are seven children in the immediate family and none of the others are affected with the condition.

Briefly, then, this patient and his mother have a condition which is characterized by acute inflammatory swelling of the legs, associated with constitutional symptoms and resulting in a permanent edema. There is no disease of the circulatory organs or of the renal organs nor any other obvious cause for the edema.

This remarkable condition was first described by Milroy, of

Omaha, in 1892. He reported a family in which of 97 individuals in six generations 22 were affected by this condition. Shortly afterward similar cases were reported by Meigs in France and by Rolleston in England. A very excellent summary of the condition was published by Hope and French in the *Quarterly Journal of Medicine*, 1907, Volume I, page 312. These authors traced a family through five generations, and found 13 out of 42 members affected. Hope and French seem to be the first to have given an accurate account of the acute attacks of inflammation and swelling of the legs associated with constitutional symptoms. In this country Fairbanks, Phillips, Griffith, and Newcomer have described typical cases.

Briefly, the characteristics of the condition are: (1) that the disease runs in families; (2) that there is no apparent cause for the edema; (3) that the edema is restricted to the legs; (4) that the condition is painless except in the acute attacks, and does not interfere with the activity of the patient, provided the legs are carefully bandaged; (5) the permanence of the edema once it is established, and (6) the remarkable acute attacks that occur in many patients, similar to the attacks shown by this boy and his mother. The condition is perfectly compatible with a long and useful life.

The pathology of the disease is not at all understood. The acute attacks certainly have all the objective characteristics of a severe lymphangitis. Many authors incline to the view that the condition is due to a vasomotor neurosis. No definite pathologic changes in the veins or the lymphatics have so far been demonstrated. The acute attacks suggest a severe generalized infection, but apparently death has never occurred during an attack. There is no treatment for the condition except palliative measures for the acute attacks and compression bandaging during the interval.

CLINIC OF DR. THOMAS R. BROWN

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SOME GASTRO-INTESTINAL NOTES

1. The Cause of the Symptoms of Gastroptosis—the Significance of a Congenitally Fixed High Duodenum and of Duodenal or Pyloric Adhesions, and the Value of Pyloroplasty in the Treatment of such Cases.

2. Visceroptosis and Chronic Appendicitis.

3. The Medical After-care of Surgical Patients After Abdominal Operations.

1. THE CAUSE OF THE SYMPTOMS OF GASTROPTOSIS—THE SIGNIFICANCE OF A CONGENITALLY FIXED HIGH DUODENUM AND OF DUODENAL OR PYLORIC ADHESIONS, AND THE VALUE OF PYLOROPLASTY IN THE TREATMENT OF SUCH CASES

IT would seem almost a work of supererogation to write anything on visceroptosis—a subject discussed from almost every angle during the past few years, when many of the ills of body and even of mind have been ascribed to this abnormality, some attempting to explain the symptoms purely on mechanical or orthopedic lines, others laying more stress on deviation from the normal in intestinal chemistry and bacteriology. Those of us who have studied these cases with peculiar care, especially those with large fluoroscopic experience, are a bit saddened by the protean symptom-complex ascribed to this condition, even in its minor manifestations, for we know too well that even great variations from the so-called normal position of the abdominal viscera may be compatible with perfect health, and that in certain very healthy people a tendency to a low position of the

viscera is almost the rule, and yet with no especial tendency to impairment of general or of digestive tone. Yet, speaking broadly, this body type is more fragile than its opposite—that of the wide costal angle and horizontal ribs—it is more likely to break down under the strain of the careless dietetic habits of the day, especially overeating and too rapid eating, and, of course, it is for this reason that prophylaxis, notably respiratory and abdominal exercises and measures to increase body weight and body tone, are of such importance in those with this, in the vast majority of cases, congenital abnormality of body form. It has always seemed to us also that in the treatment of the more advanced cases, where the descent is marked and is definitely associated with many symptoms, notably in the digestive sphere, far too much attention has been paid to fattening cures and artificial supports, far too little to the much more physiologic measures directed toward really correcting the underlying causes by exercises designed to increase the cubic contents of the hypochondrium, to strengthen the spine, and to straighten the back—though in this field certain of our orthopedic brethren have done splendid work—and to increase the tone of the abdominal musculature by appropriate measures, mechanical, dietetic, even psychic, as there is a peculiar association, though not necessarily of especial etiologic significance, between this abnormal body form and a fragile, unstable nervous system.

But it is not the general subject of visceroptosis that we wish to present, but rather certain local features which have seemed to us of especial interest and peculiar significance, both as regards symptomatology and therapy in certain phases of this subject. To us no problem to be unravelled in the domain of visceroptosis is of greater interest than the *raison d'etre* of the symptoms in gastroptosis and its appropriate therapy. Certain cases of the highest grade of gastroptosis will present no symptoms; others will present symptoms of great variety, ranging from those of a simple functional dyspepsia, with fulness and discomfort after meals and other symptoms of slight atony, to obstructive phenomena and definite pain—enough to

make one strongly suspect pyloric ulcer. Obviously, if pylorus and duodenum drop with the rest of the viscera there should be no materially increased difficulty of emptying, and unpleasant symptoms should not supervene, while if duodenum and pylorus remain in approximately their normal positions the actual emptying is rendered much more difficult, especially in the upright position. What are the conditions which lead to this high position of stomach and duodenum with descensus of the rest of the viscera? In our experience, based on several thousand fluoroscopic studies, the cause is, in the vast majority of cases, either one or the other of two, sometimes both playing a rôle in the individual case—one a congenitally fixed high duodenum, present, in our experience, in approximately 50 per cent. of the cases, and the other, conditions associated with the formation of adhesions in the region of the pylorus, duodenum, and gall-bladder, pos ibly secondary to a cholecystitis, possibly to an erosion of duodenal or pyloric mucosa. In many of these cases these must be regarded as being metastatic in origin from infections in tonsils or sinuses, at the base of the teeth, or certainly in the larger number from diseased conditions in lower levels of the digestive tract—notably appendix, cecum, or ascending colon, when a reflex pylorospasm from a constant or intermittent reflex stimulation and its consequent disturbance in blood and lymph supply of gastric and duodenal mucosa also play a part in lowering resistance, and often in producing definite although microscopic injury to the mucous membrane. If the ptosis is not marked, and the strain on the stomach from overeating and overdrinking is not great, the symptoms may be *nil* or practically *nil;* but if the descensus is very great, or the burden placed upon the stomach too severe, in either case—congenital high fixation or that due to adhesions—symptoms will sooner or later appear, the stomach will have increasing difficulty in emptying, especially in the upright position, and obviously much more with constant overloading, and first hypertrophy and hypertonicity will develop, and later atony and dilatation with increase in symptoms, due to difficulty in food propulsion through the narrowed opening, pylorospasm, and partial pyloric obstruction.

Nothing demonstrates more beautifully the underlying mechanism of such a condition than the fluoroscopic study of these cases in the prone and in the upright position; in the former the irritative or obstructive phenomena being minimized, with comparative ease of emptying; in the latter being present to a marked extent, singularly like the picture of gastric ulcer, with its relationship to quality and quantity of food and to time of appearance of symptoms after a meal.

These cases are peculiarly resistant to the ordinary modes of treatment, especially if the persistent irritation and dragging or contraction of adhesions shall have led to a true organic pyloric stenosis. Posture, weight increase, rest after meals, supports, measures designed to increase the tone of the gastric and abdominal musculature, to enlarge the hypochondriac space, to strengthen the pelvic floor, with a diet and mode of life based on the physiologic requirements, will, of course, help, and sometimes markedly, in lessening symptoms; but in most cases of the highest grade permanent improvement is extremely difficult by these means, nor will an operation for the separation of adhesions be more than ephemeral in its benefits because of the almost inevitable early re-formation of adhesions, even with the most careful technic, great care to avoid trauma, and interposition of the omentum between the raw surfaces. Gastropexy and gastroplication are both frail reeds on which to lean, and it is, therefore, in this group of cases—so intractable to treatment, so peculiarly liable to relapse after apparent improvement—that for the past few years we have advised a pyloroplastic operation. According to our viewpoint this is the ideal treatment for the condition presented, for it removes the one great obstacle to success in other forms of treatment; it substitutes a wide, competent opening for a narrow one contracting still further, it reduces the element of spasm to a minimum, and relieves the tendency to increased stasis in the simplest and most physiologic manner without impairing the freedom of the movements of the stomach so definitely affected in any operation of fixation of this organ. We have had a number of such cases so treated in the past few years, cases absolutely

resistant to the usual methods, and the results have been singularly gratifying in practically all instances. Perhaps the fact that Dr. Finney, the originator of pyloroplasty, was the surgeon in most of the cases (although he was at first rather skeptical as to its applicability in this group of cases, but was subsequently convinced of the good results obtained thereby) added immensely to the patient's chance of ultimate recovery, as success is to be expected only if the operative results are ideal, with no subsequent contraction of the opening. Most of the failures met with after this operation, whatever the condition for which it is performed, may be explained by faulty technic on the part of the surgeon in the execution. With a perfect technic, however, we feel that it affords the best method of relieving the symptoms in this group of cases, combined, of course, with proper after-care and a realization of the inherent abnormality, which is to be discounted as far as possible by a careful mode of life, especially as regards habits of eating.

2. VISCEROPTOSIS AND CHRONIC APPENDICITIS

We shall not touch here upon the many cases of chronic appendicitis secondary to acute or subacute inflammation of this organ, cases in which in many instances a most careful history running back into early childhood may be necessary to disclose that there were acute conditions ever present—long forgotten attacks of pain in the right side or repeated attacks of colic in childhood or even babyhood, only discovered after very careful questioning, being the only obvious expressions of acute appendical inflammation. Even in this group of cases, when the acute stage is a thing of the past and when the only symptoms remaining are those both local and reflex due to cecal stasis, thickened and twisted appendix, it is extremely problematic as to the wisdom of suggesting surgical treatment—as many of us have too often discovered to our cost.

But we wish here to discuss a different type of chronic appendical and periappendical inflammation, a type chronic from the first, with no acute stage, met with with peculiar frequency in high grades of visceroptosis. In the first place, that there is a

definite relationship between visceroptosis and chronic appendicitis seems to us to be beyond peradventure, and yet it is very likely to be misinterpreted. Our feeling has been that in this group of cases the appendicitis is in no sense primary, but simply represents one phase of a low-grade inflammatory process, of which perityphlitis, pericolitis, and possibly such conditions as Jackson's veil or Lane's band are other manifestations, an inflammation probably brought about by disturbances of blood and lymph supply inevitable to such high grades of displacement, with, as a possible additional factor, a low grade of toxemia or bacteremia due to the stasis and fecal retention. The real tragedy in these cases is the usual lack of realization that this appendical inflammation is but a part of this low-grade inflammatory process involving not only the appendix, but the terminal ileum, cecum, ascending colon, and sometimes even the first portion of the transverse colon, and, not realizing this relationship, the unfortunate tendency of so many physicians to ascribe all the symptoms to the chronic appendicitis, so easily recognized by local signs and symptoms and by fluoroscopic study, and with its discovery urging operative removal in the belief that by so doing the symptoms may be relieved—a dream that is rarely realized, a chimera that too soon fades away with the return of many or all of the original symptoms.

Our feeling has always been that in high grades of visceroptosis with fecal stasis, in which the appendix can be proved to be definitely diseased, it is, as a rule, worse than useless to remove it, for the postoperative adhesions which usually form, though, of course, lessened by the better surgical care now in vogue in many hospitals, often lead to an increase in fecal retention and a diminution in lower bowel tone and peristalsis that makes the second state of that man—or oftener woman—worse than the first. After all, to expect the removal of what is but an effect and not the primary cause to clear up a picture in the development of which disturbances—secretory, motor, and sensory—of the gut play important rôles, as well as marked variations from the normal intestinal bacteriology, is chimeric to say the least. And so let us not be too optimistic when, after fluoroscopic ex-

amination or *x*-ray plate, the patient is told that he has a chronic appendicitis with visceroptosis, and that the appendical removal will be all-healing in its effects. The surgeon who removes the often comparatively quite innocent organ and then sees the patient no more may have this delusion, but not the medical man to whom the patient so often returns in three or six months with the same complaints. We should not like to say how many patients we have seen during the past few years in whom after appendectomy the symptoms, both local and reflex, have returned—the cecal stasis, the pericecal thickening on the one hand, the hypersthenic stomach with pylorospasm, hyperchlorhydria, or hyperchylia on the other. It is but another example of the all too frequent tendency of the day to attempt to explain all the symptoms of any case by the one organ or tissue found diseased, and to expect its removal to bring about a cure.

3. THE MEDICAL AFTER-CARE OF SURGICAL PATIENTS AFTER ABDOMINAL OPERATIONS

Perhaps nothing in the history of surgery has been more striking than its brilliant success in acute abdominal conditions. But this is proving a two-edged sword, in a way, because it has persuaded most of the laity and many clinicians that surgery is omnipotent even in chronic abdominal conditions. If surgery had solved with complete satisfaction these latter conditions, which are obviously surgical in nature, such as ulcer with obstruction or adhesions, gall-bladder disease, abdominal adhesions, and chronic appendicitis, no one could complain. But it is in just these cases that surgery cannot promise a complete cure; and it is the many failures to give complete or even any relief in many of these cases that warrant our persistence in attempting to treat them at all by other than surgical means.

Are there any means at our command to lessen the percentage of failures in this group of cases treated surgically, and what are the main reasons for such failures? Broadly speaking, the one great cause for failure in abdominal operations is the tendency toward the formation of adhesions in this group

of cases, a tendency partly depending, of course, upon the technic of the surgeon, but also to a very great extent upon individual idiosyncrasy. What means have we at our command to lessen this tendency? For the past few years in many of our abdominal cases which have come to operation, especially those in which conditions peculiarly favorable to adhesion formation were met with, we have insisted upon what has been facetiously called by some our rocking-horse treatment, having the patient's position frequently changed from side to side—with alternate elevation of the foot and head of the bed, early and frequent use of laxatives, massage begun as soon as possible and continued for a considerable time, and if impossible on account of the expense, as a substitute automassage with a 3- or 5-pound cannon-ball, and from very careful studies, especially those under the fluoroscopic screen, we are absolutely convinced that adhesion formation can be minimized by this method. We cannot insist too strongly upon the value of these measures to minimize adhesion formation. We have been able to follow a large number of cases so treated over long periods of time and to verify the results with careful and frequent fluoroscopic studies, studies which told us better than anything else how easy it is to change the position of the abdominal viscera by change of posture of the patient or by massage, studies which should make us realize the value of these methods in lessening adhesion formation.

Another point of fundamental importance in the after-care of surgical abdominal patients is the proper regulation of the diet. For the first few days the problem is, of course, very simple—starvation, then water, then simple liquid foods, and then a bland soft diet, and by these means no harm is likely to result. The fatal mistake occurs only too often in not differentiating these patients as regards diet when the stage of solid food is reached. To give the same diet after pyloroplasty, gastroenterostomy, gall-bladder operation, or gastric resection as we would after operations for fracture of the thigh or cancer of the breast shows a basic ignorance of the pathologic physiology of the former group of cases. We should remember that hyper-

acidity remains long after the underlying cause has been removed; and it is tempting Providence, to say the least, to ply these patients with tomato soup, salad dressing, and coarse food in the early stages of their convalescence. After gastro-enterostomy very abnormal conditions must supervene. The jejunum, habituated as it is to receive only liquid or almost liquid chyme of alkaline reaction, under the new conditions receives food, frequently very acid, directly from the stomach through the new opening. It is essential, if the danger of producing jejunal catarrh or jejunal ulcer is to be reduced to a minimum, that a very simple, soft, well-chewed, and carefully chosen dietary be persisted in for a very long period of time if the maximum success is to be expected, as after an operation so fundamentally unphysiologic it is only by these means that persistent intestinal troubles can be avoided.

After cholecystectomy chronic persistent diarrhea is so likely to occur that it is of paramount importance that a proper dietary be insisted upon over a long period of time and until the optimum condition of bile discharge and pancreatic flow has been established. Certainly, except for purely surgical complications the after-care of these cases of abdominal operation would be fraught with greater success than if they were left entirely in the hands of the surgeons. In this day the surgeon may be God's anointed, but in the matter of after-care of patients after abdominal operations, especially as regards dietetics, he is neither omnipotent nor omniscient, and many of his complete or partial failures might have been avoided by avoiding routine postoperative treatment and by formulating an individual therapy based on the secretory, sensory, and motor problems presented in each individual case.

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